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FROM THE INSTITUTE OF PEDIATRICS "G. GASLINI"-UNIVERSITY OF GENOVA (ITALY), DIRECTOR: PROF. G. DE TONI, AND THE INSTITUTE OF RADIOLOGY OF THE UNIVERSITY OF GENOVA (ITALY), DIRECTOR: PROF. A. VALLEBONA.

The Simultaneous Visualization of the Posterior and Anterior Mediastinum after Insufflation in the Peridural Space. Tridimensional Tomographic Study

by

G. SANSONE and A. DE MAESTRI

Introduction

While the problem of the radiographic visualization of the structures of the anterior mediastinum has received brilliant solution with the technic suggested by CONDORELLI (1936), investigations on the posterior mediastinum still remain very difficult, especially in the pediatric field. The gaseous insufflation after transtracheal puncture (CONDORELLI, 1949) was not considered suitable by us for children. Therefore we thought that the intrarachidian extradural way, by means of an injection of a gaseous contrast medium into the peridural space, would be more satisfactory. This procedure has been already tried in the past, but it was never applied for clinical purposes. We perfected the method so that the results now are almost always constant.

Technic

The child sits on the bed in the lumbar puncture position. A short needle, 4 cm long, with stilet is introduced between the XI and the XII dorsal vertebra in the middle line, as for a spinal puncture. The introduction must be stopped when one has the impression that the yellow ligament has been passed. Then with

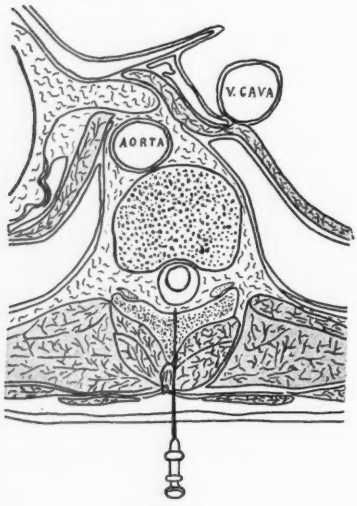

Fig. 1.

a large syringe (50 or 100 cc) the gas is injected: we still prefer oxygen. It is advisable to leave the needle "in situ", in case more gas is required. During the operation the child can keep his seated position. Sometimes we obtained good results with the child in the lying position on the right side with a pillow transversally placed.

The gas escapes through the intervertebral foramina, reaches the loose prevertebral connective tissue and outlines all the anatomical structures of the mediastinum (Fig. 1). After a fluoroscopic examination, plain anteroposterior and lateral films and later on anteroposterior, lateral and transversal axial tomographies are performed. The maximal quantity of injected oxygen in older children was 500—600 cc. No disturbances occurred in our patients, except sometimes a slight subcutaneous emphysema in the lateral cervical or dorsal region or a very moderate infiltration in the neck. An observation of interest was that the gas reaches the anterior mediastinum usually from the posterior mediastinum giving a marked retrosternal emphysema. The presence of the gas in the thorax lasts only a few hours.

Radiological pictures

Plain anteroposterior films. The injected gas appears localized in the paravertebral regions as a thin longitudinal strip. When insufflation is more advanced, the heart borders become sharply outlined and separated below from the diaphragm. *In lateral films* the cardiac silhouette is sharply delimited in its outline and separated very well from the thoracic anterior wall. The isolated thymus is sunk in the retrosternal emphysema. The aorta is visible in all its thoracic course, even if partially obscured by superimposed shadows (Fig. 2). Tomography, allowing the dissociation of the shadows, gives a more clear cut visualization of the various mediastinal structures. In *anterior tomographic films*, on different layers, the thoracic descending aorta, the aortic arch, the pulmonary conus, the ascending tract of the aorta, the thymus can be visualized. *In lateral tomographic films*, following the layers from the right to the left side, we can see the pulmonary branches of the right pulmonary artery, the cardiac silhouette sharply outlined and the ascending aorta, the aortic arch and the pulmonary conus, the thoracic descending aorta and the branches of the left pulmonary. Very interesting are the tomographic examinations performed in *axial transversal projections*, with which the aorta in all the thoracic course and — in the superior layers — the descending vena cava, the innominate, the carotid and the subclavian arteries, besides naturally the thymus separated from the vascular formations, are clearly visualized (Figs. 3—4).

Conclusion

Following personal experience, we can state that the method of gaseous insufflation in the peridural space through the intrarachidian extradural way is an ideal procedure in pediatrics, which allows a simultaneous and sharp visualization both of the anterior and of the posterior mediastinum. It is easy, safe and well tolerated by children. In association with tomography (in anteroposterior, lateral and axial transversal projections) this method gives the possibility of very interesting tridimensional pictures. We

can foresee therefore a wide application of this technic for the radiological diagnosis of mediastinal morbid conditions. In the study of congenital heart diseases it will represent, in association with other technics, an invaluable method of investigation.

La mise en évidence simultanée du mediastin postérieur et du mediastin antérieur par insufflation gazeuse dans l'espace péridural. Etude stratigraphique à trois dimensions.

Les auteurs montrent que la méthode de l'insufflation gazeuse dans l'espace péridural par voie intrarachidienne extradurale est un procédé idéal en pédiatrie, qui réalise une mise en évidence simultanée et nette du mediastin antérieur et du mediastin postérieur. Cette méthode est facile, sans risques et est bien tolérée par les enfants. Associée à la stratigraphie (en position antéro-postérieure, latérale et transversale) cette méthode offre la possibilité de faire de très intéressantes images à trois dimensions.

Die gleichzeitige Sichtbarmachung des Mediastinum post. und ant. nach Insufflation in den Periduralraum. Dreidimensionale tomographische Studie.

Die Verfasser geben an, dass die Methode von Gaseinblasung in den Periduralraum durch den intrarachidischen extraduralen Weg ein ideales Verfahren der Pädiatrie ist, welches eine gleichzeitige und scharfe Sichtbarmachung sowohl des vorderen als des hinteren Mediastinums erlaubt. Es ist leicht und sicher und wird gut von Kindern vertragen. In Verbindung mit Tomographie (mit anteroposteriorer, lateraler und axialer transversaler Projektion) gewährt diese Methode die Möglichkeit sehr interessanter dreidimensionaler Bilder.

Visualización simultánea del mediastino anterior y posterior tras insuflación del espacio peridural. Estudio estratigráfico tridimensional.

Los autores son de la opinión que el método de insuflación gaseosa del espacio peridural a través de la via intraraquídea extradural es un procedimiento ideal en pediatria el cual permite una clara y simultánea visualización del mediastino anterior y posterior. Es un procedimiento fácil, cómodo y bien tolerado por los niños. En asociación con la estratigrafía (en proyecciones anteroposterior, lateral, y axial transversa) este método proporciona la posibilidad de obtener imágenes tridimensionales de alto valor.

Fig. 2. Lateral projection: heart, aorta, thymus are visualized.

Fig. 3. Axial tomography, superior layers.

Fig. 4. Axial tomography, lower layers.

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FROM THE CHILDREN'S CLINIC OF THE UNIVERSITY, HELSINKI.
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The Weight of the Thyroid Gland in Children of 0—2 Years of Age

by

HILKKA TÄHKÄ

In investigations of the adrenals of children of 0—2 years of age, for purposes of comparison with thyroid glands the author removed and weighed them at autopsies. As the changes in weight of the thyroid glands in children of this age have not previously been investigated in Finland in an extensive series, it is justifiable to publish the results obtained. At the same time it was considerable useful to study the effect of diseases of different type and duration on the weight of the thyroid gland or whether it is to be assumed that the size of the thyroid gland is mainly determined by the presence of endemic goitre. The paper also gives some indications of the frequency of goitre in Finnish children of this age.

Material and Methods

The thyroid glands were collected from the same material as the thymuses, which have been discussed in the author's previous work on thymus, in this issue of Acta Paediatrica.

The material comprises 244 cases. 80 of the infants (41 male and 39 female) were prematurely born and 164 (91 male and 65 female) were fullterm infants.

The thyroid gland was weighed in each case to an accuracy of 0.01 g.

In the present material the mathematical treatment is based on the same principles as in the work concerning the thymuses.

Changes in the Weight of the Thyroid Gland

Foetal development

CLATWORTHY & ANDERSON (1944), described the increase in the weight of the thyroid gland in the foetus. Their results are based on the values of JACKSON and SCAMMON, and on values collected by JACKSON from the literature. The weights of the thyroid gland in foetuses of 75—2500 g, published by EKHOLM & NIEMINEVA from Finland, coincide fairly well with the values given by CLATWORTHY & ANDERSON. Of their results, the weights of the thyroid gland of foetuses from the immature stage (birth weight 600—1249 g) onwards are particularly interesting in this connection (Table 1).

Table 1.

The weights of the thyroid gland of foetuses weighing 600—2500 g, according to EKHOLM & NIEMINEVA.

Weight of foetus (g)	Number of cases	Weight of thyroid gland (g)	Relative weight of thyroid gland
600—1 249	14	0.95—1.9	1 : 646 or 0.15 %
1 250—2 500	16	1.65—3.18	1 : 671 or 0.15 %

EKHOLM & NIEMINEVA particularly stress that individual variations in the weight of the thyroid gland are remarkably great.

Postnatal development

Table 2 shows the average weights of the thyroid gland of newborn infants according to several investigations.

As is shown by Table 2, the average weight of the thyroid gland in different localities varies considerably even in the newborn. When studying the subsequent changes in the weight of the thyroid gland it must also be borne in mind that the materials of the different investigators are not comparable because of the variability of the incidence of endemic goitre.

According to UOTILA, the weight of the thyroid gland in Finnish children increases as follows (Table 3). Definite cases of goitre have been excluded.

The values given by the Italians, CASTALDI & VANNUCCI, are given in Table 4.

Table 2.

The weight of the thyroid gland in newborn infants.

	Weight of the thyroid gland (g)		Relative weight of the thyroid gland (%)	
	Male	Female	Male	Female
HIILESMAA (Finland)	2.4			
LEIDENIUS »	3.0			
UOTILA »	2.9	3.3	0.09	0.10
CASTALDI & VANNUCCI (Italy)	2.25	2.22		
HESSELBERG (Kiel)	1.5			
HUECK (Leipzig)	1.2			
KOCH (Lund)	2.2			
WEGELIN (Bern)	8.2			
» (Kiel)	1.9			
» (München)	6.0			

Table 3.

The development of the weight of the thyroid gland according to UOTILA.

Age	Weight of the thyroid gland (g)			
	Male	Number of cases	Female	Number of cases
Newborn	2.9	89	3.2	67
0—6 months	3.5	1	3.2	2
7—12 »	5.5	2	—	—
1 year	5.5	2	7.0	1
2 years	6.5	1	6.0	1

YLPPÖ has found that the thyroid glands of premature infants are remarkably small. HIILESMAA demonstrated the same in his series. The changes in the weight of the thyroid in premature infants has not been found in the literature.

Table 4.

Changes in the weight of the thyroid gland according to CASTALDI & VANNUCCI.

Age	Weight of the thyroid gland in g		
	Male	Female	Range
8—9 foetal months.....	1.48	1.44	0.41—1.94
Newborn	2.25	2.22	1.23—3.86
0—4 months	1.66	1.29	0.94—3.33
4—7 »	1.21	1.09	1.07—1.31
7—12 »	1.99	2.05	1.44—3.25
1—2 years	2.74	2.74	1.41—7.01

Present Investigations

Fullterm infants

The average weights of the thyroid gland in the different age groups are given in Table 5. In calculating these values all thyroid glands exceeding 6.00 g in weight have been excluded

Table 5.

Weight of the thyroid gland in different age groups.

Age	Weight of thyroid gland (g)		Number of cases
	Average	Range	
0—7 days.....	3.00±0.11	1.48—5.48	23
8—14 »	3.20±0.48	1.28—5.42	8
15—30 »	3.04±0.24	1.62—4.72	11
1—2 months	2.45±0.45	0.98—5.70	11
2—3 »	2.03±0.26	0.97—5.70	18
3—4 »	2.27±0.20	1.43—3.32	15
4—5 »	2.42±0.26	1.60—5.75	16
5—6 »	3.52±0.30	2.00—4.99	11
6—9 »	2.91±0.24	1.48—5.95	20
9—12 »	3.28±0.32	1.20—4.45	11
1—2 years	2.55±0.24	1.80—3.88	10

as this value, according to LEIDENIUS and UOTILA, must be considered the goitre limit in Finland.

It would seem that the weight of the thyroid gland (Table 5) undergoes hardly any change in the course of the first month of life. The average value of approximately 3 g is that found by UOTILA and LEIDENIUS in the newborn. After the first month the weight of the thyroid gland is reduced, attaining its minimum value of 2.03 g, or 68 per cent of the newborn value, in the age group 2—3 months. Calcules of correlation show that this decrease of the thyroid gland is statistically significant. After this the weight of the thyroid gland begins to increase slowly, but in the age group 1—2 years the average weight is still only 2.55 g.

Premature infants

Table 6 shows the weights of the thyroid gland in premature infants, classified according to age.

Table 6.

Weight of the thyroid gland in premature infants.

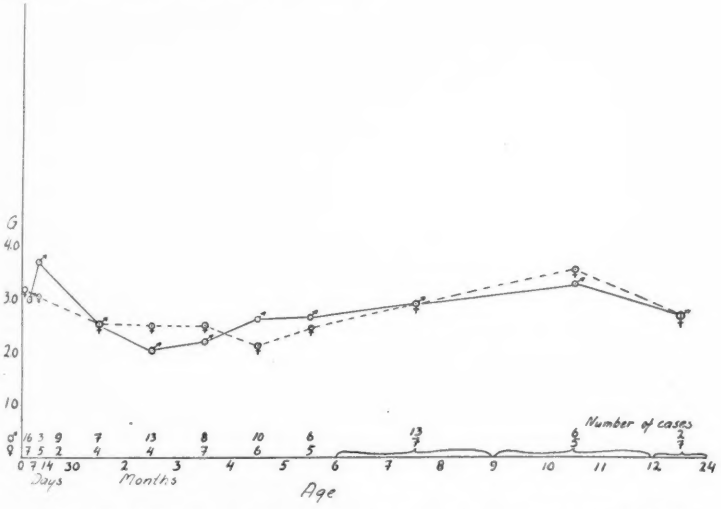
Age	Weight of thyroid gland (g)		Number of cases
	Average	Range	
0—7 days	1.90±0.14	0.82—4.90	41
8—14 »	1.90±0.30	0.55—3.82	10
15—30 »	2.02±0.50	0.51—3.98	6
1—2 months	1.43±0.40	0.72—3.00	9
2—3 »	1.95±0.57	0.11—4.82	7
3—4 »	1.12±0.10	0.77—1.43	5
4—5 »	2.52 —	— —	1
5—6 »	— —	— —	—
6—7 »	1.80 —	— —	1

The average weight of the thyroid gland in premature infants also begins to decrease after the first month. The lowest value is reached in the 3—4-month age group, and the weight of the thyroid gland is then 59 per cent of the newborn value.

On the basis of Tables 5 and 6 it can be said that the absolute weight of the thyroid gland in premature infants is distinctly lower than it is with full-term births, but that the development in the earliest months of life is on the same lines.

The weight of the thyroid gland in male and female infants

UOTILA and CASTALDI & VANNUCCI were unable to demonstrate any distinct differences in weight between the thyroid glands of male and female infants.



Graph 1. The weight of the thyroid gland in male and female full-term infants.

The average weights of the thyroid gland, in the different sexes in this investigation, for full-term infants are given in Graph 1. From it can be stated that no evident differences can be observed.

Birth-weight in correlation to the weight of the thyroid gland

CLATWORTHY & ANDERSON, YLPPÖ, HIILESMAA, etc., found that the thyroid gland increases considerably in weight during

the last weeks of pregnancy. It was, therefore, considered worthwhile examining whether any correlation exists between birth-weight and the weight of the thyroid gland. In Table 7 each group includes only infants who died within 24 hours of birth, thus excluding the possible influence of various external factors on the size of the thyroid gland.

Table 7.

Relationship between birth-weight and the weight of the thyroid gland.

Birth-weight (g)	Average weight of thyroid gland		Number of cases
	Absolute weight (g)	Relative weight (%)	
600—1 249	1.01 ± 0.07	0.10	4
1 250—1 999	1.58 ± 0.29	0.10	4
2 000—2 500	3.31 ± 0.55	0.16	4
over 2 500	3.42 —	0.12	2

It is evident that the absolute weight of the thyroid gland increases considerably towards the end of the pregnancy. It is not, however, possible to prove this statistically due to the small number of cases. The changes in the relative weight are less clear.

Congenital goitre

The limit value between goitre and a "normal" thyroid gland is taken to be, in newborn children in Finland, 6.0 g (according to LEIDENIUS and UOTILA) and 5.0 g (according to HIILESMAA). In UOTILAS report (196 cases) approximately 25 per cent of the newborn had goitre and was found to occur almost equally in girls and boys. Of 23 full-term newborn babies, HIILESMAA found a thyroid gland exceeding 5.0 g occured in six cases, while among 24 premature births there was only one such case.

According to BAADER, foetuses under 47 cm in length seldom have a goitre. On the other hand, GUGGISBERG has found thyroid glands of 11—13 g as early as the 6th—7th month of pregnancy.

In the present material 6 g is taken as the goitre limit. No mention was found in literature about the goitre limit in infancy

and early childhood. However, the limit value for the newborn is probably applicable to the entire material, because, as Table 5 shows, the average weight of the thyroid gland has not yet exceeded the newborn weight at the age of 2 years.

Among the 154 full-term births there were 10 cases (6.25 per cent), where the thyroid gland exceeded 6.00 g in weight. Of 80 premature births goitre was not found in a single instance.

Table 8.

The cases of goitre.

Case No.	Sex	Age	Diagnosis	Weight of thyroid gland g
183/49	♀	20 min.	Anencephalus	8.73
130/49	♂	5 days	Vitium cordis cong.	6.54
100/49	♀	11 »	Septicaemia	7.50
53/49	♂	28 »	Haematoma subdurale	6.36
146/49	♂	1 month	Vitium cordis cong.	8.02
354/48	♀	2 1/2 months	Gastroenteritis	7.60
113/49	♀	2 1/2 »	Vitium cordis cong.	15.82
400/48	♂	5 1/2 »	Tub. miliaris	27.50
11/49	♀	5 1/2 »	Debilitas cong.	19.72
135/49	♂	5 1/2 »	Pneumonia	6.57

Table 8 shows the cases of goitre. In this small group there is no difference between the sexes (5 female and 5 male infants). Meriting attention probably is the fact that, of the 10 goitre patients, congenital heart malformation was the main cause of death in 3. Infants with this disease totalled in all 15.

The influence of various factors on the size of the thyroid gland

JACKSON found that in acute starvation the weight of the thyroid gland of the test animals undergoes no considerable changes, but that chronic malnutrition reduces it by some 22 per cent. KENYON showed that lengthy exposure to cold causes increase in the size of the thyroid gland, and produces signs of increased activity in the histological structure. SELYE found that fairly slight changes are present in the thyroid gland in connection with the "General Adaptation Syndrome." In

some cases, however, he has found thyroid atrophy at the shock stage of the alarm reaction, and indications of increased activity in counter shock and at the stage of resistance. UOTILA & PEKKARINEN have shown that signs of increased activity are present in the thyroid gland of men who have died suddenly. CROOKE & GILMOUR found that the removal of the pituitary causes reduced activity both in the thyroid gland and the adrenal cortex. Similar findings were also reported by INGLE & HIGGINS and DEANE & GREEP in their experiments.

No mention has been traced in literature on the influence of diseases of different kinds and of different duration on the size of the thyroid gland.

The influence of the duration of disease on the weight of the thyroid gland

Table 9 gives the weights of the thyroid gland as a function of the duration of disease. The cases of goitre have been excluded. The same applies to premature births as, with the majority of them, the age equals the duration of disease.

Table 9.

Weight of the thyroid gland as a function of the duration of disease in full-term infants.

Duration of disease	Weight of thyroid gland in g		Number of cases
	Average	Range	
0—3 days.....	3.24±0.20	1.63—5.48	24
4—7 »	2.81±0.25	1.28—5.70	28
8—14 »	3.40±0.36	0.97—5.75	15
15—30 »	2.73±0.24	0.74—5.70	27
1—2 months	2.24±0.16	0.98—3.90	25
2—3 »	2.43±0.42	0.70—5.95	13
3—4 »	2.27±0.47	1.43—5.63	9
4—5 »	1.66±0.09	1.48—1.85	5
over 5 »	2.81±0.26	1.53—4.10	8

It would seem as if the weight of the thyroid gland (Table 9) in patients who died after a disease of short duration were

somewhat higher than in those who had been ill for a long time. However, the differences are so small that, according to correlation calculations, they are not statistically significant.

Of the individual disease groups, only the group of deaths from gastroenteritis is large enough (49 cases) to justify a more detailed analysis. This group, furthermore, is of interest in that the children belonging to it are generally in a condition of malnutrition and have, in cases where the disease has been of long duration at least, lived on an insufficient diet. For comparison with these diarrhoea patients, a so-called miscellaneous group was used, comprising all the other cases. For sake of uniformity, however, all patients under 15 days of age were excluded, as the youngest baby dying of gastroenteritis was 15 days old. Table 10 gives the diarrhoea and miscellaneous groups classified according to the duration of disease.

Table 10.

Weight of the thyroid gland as a function of the duration of disease in the gastroenteritis and miscellaneous groups.

Duration of disease	Average weight of thyroid gland in g		Number of cases	
	Gastroenteritis	Miscellaneous	G—e	Misc.
0—3 days.....	3.45±0.40	3.05±0.34	5	7
4—7 »	3.00±0.60	3.19±0.30	7	9
8—14 »	2.47 —	3.33±0.60	2	7
15—30 »	2.56±0.31	2.94±0.37	15	12
1—2 months	2.25±0.24	2.23±0.20	12	13
2—3 »	2.61±0.87	2.33±0.46	5	8
3—4 »	1.71 —	2.43±0.54	2	7
4—5 »	— —	1.66±0.10	—	5
over 5 »	2.80 —	2.82±0.26	1	7

A comparison of the diarrhoea and miscellaneous groups shows that no significant differences can be distinguished in the weights of the thyroid gland.

Deviation percentage of the weight of the thyroid gland from the "normal" weight as a function of duration of disease

The absolute weights of the thyroid gland in relation to the duration of disease have been discussed above. The results are somewhat indefinite due to the fact, as shown by Table 5, the weight of the thyroid gland varies in the different age groups, and that the number of infants of different ages compared with disease duration groups is completely haphazard.

To clarify the matter, a calculation was made in each case to show how much the thyroid gland deviates from the so-called normal weight for the age in question; the average values of these deviations have been calculated by groups of disease duration. There being no true normal cases available, it has been necessary to employ as "normal values", the average weights of thyroid gland shown in Table 5.

The following denominations have been used: normal value = 0, and the deviations are given as + or — percentages of this value.

Table 11 gives these results; infants under 15 days of age are excluded.

Table 11.

Deviations of the weight of the thyroid gland as percentages of the so-called normal weight, by groups of disease duration.

Duration of disease	Deviation from normal value (%)		Number of cases
	Average	Range	
0—3 days	+17.6	—63—+ 95	12
4—7 »	+16.6 +15 ±6.2	—60—+130	16
8—14 »	+ 9.2	—58—+ 90	9
15—30 »	+ 4 — 2.6±5.6	—63—+180	27
1—2 months	— 9.8	—63—+ 40	25
2—3 »	— 5.4	—65—+100	13
3—4 »	— 6.8	—57—+ 95	9
4—5 »	—43 —10.6±6.6	—57—— 30	5
over 5 »	— 3.6	—48—+ 30	8

It seems that the size of the thyroid gland (Table 11) is reduced the greater the duration of disease. A statistical analysis of the results shows that this is statistically significant.

The relationship between the weight of the thyroid gland and the weights of the adrenals and the thymus has been reported elsewhere.

Comment

As is well-known, the size of the thyroid gland is considerably affected by local endemic goitre. As, in the present series, no distinct relationship can be seen between the absolute weight of the thyroid gland and age, duration of disease or type of disease, it can be assumed that the considerable individual variations observed in the size of the thyroid gland can be explained as the result of different endemic goitres. The patients of the Children's Clinic come from all over Finland, and the endemic goitre varies in intensity in the different regions.

Congenital goitre was found in 6.25 per cent of the full-term births in the present material. In UOTILA'S and HIILESMAA'S series the goitre percentage in the newborn was about 25. Obviously slight goitres of the newborn disappear with age.

In calculating the size of the thyroid gland as a percentage of the average weight for the same age, it would seem that the thyroid gland is at its largest in patients who have died of an acute disease, and decreases with the length of duration of disease. This might lead to the presumption that in chronic diseases the activity of the thyroid gland or the pituitary governing its activity is weakened. However, no conclusions as to the activity can be drawn from the size of the thyroid gland alone; a histological investigation would be necessary.

Summary

1) The thyroid glands of 244 infants of 0—2 years who had died of different diseases was examined and weighed.

2) The results show that the absolute weight of the thyroid gland is roughly constant, approximately 3 g for the whole of the first month of life. Subsequently, the weight begins to decrease reaching its min-

imum value (approximately 68 per cent of the newborn), at the age of 2—3 months. From that age the weight again begins to increase slowly.

3) The changes in weight are along the same lines in premature infants, the absolute weights only being considerably lower as, a fact evident from this series too, the size of the thyroid gland increases greatly towards the end of pregnancy.

4) No difference can be shown between the sexes in the size of the thyroid gland.

5) Congenital goitre was found in 10 patients of the material, i.e., in 6.25 per cent. In premature infants not a single case of goitre was encountered.

6) The duration and type of disease cannot be shown to affect the absolute weights of the thyroid gland. On the other hand, the size of the thyroid gland, calculated as a percentage of the average weight for the same age, seems to decrease the longer the duration of disease.

Le poids de la glande thyroïde chez les enfants de 0 à 2 ans.

1) On a autopsié et pesé la thyroïde de 244 enfants âgés de 0 à 2 ans, qui sont décédés par suite de maladies diverses.

2) Les résultats montrent que le poids total de la glande thyroïde est assez constant, environ 3 gr. pendant tout le premier mois de la vie. Par la suite, le poids commence à décroître pour atteindre à l'âge de 2 à 3 mois sa valeur minimum soit approximativement 68 % du poids de la glande chez le nouveau-né. A partir de cet âge le poids augmente à nouveau doucement.

3) Le développement se fait d'après le même schéma chez les enfants prématurés, les poids totaux étant considérablement plus petits, ainsi qu'il semble démontré par l'examen de ce matériel, la glande thyroïde se développant beaucoup vers la fin de la grossesse.

4) On ne relève aucune différence entre les sexes quant à la grandeur de la glande thyroïde.

5) Dans le matériel examiné on a trouvé 10 cas de goître congénital, c.à.d. dans 6,25 % des cas. Chez les prématurés on n'a pas rencontré un seul cas de goître.

6) On n'a pas pu démontrer que la durée ou le type de maladie donnée pouvait affecter le poids total de la glande. D'autre part la grandeur de la glande thyroïde, calculée en % du poids moyen du même âge, semble décroître quand la maladie se prolonge.

Über das Gewicht der Schilddrüse bei Kindern von 0—2 Jahren.

1) Die Schilddrüse von 244 Kindern im Alter von 0—2 Jahren, die an verschiedenen Krankheiten gestorben waren, wurde obduziert und gewogen.

2) Die Resultate zeigen, dass das absolute Gewicht der Schilddrüse während des ganzen ersten Lebensmonats ungefähr konstant ist, approx. 3 g. Danach beginnt das Gewicht abzunehmen und erreicht seinen niedrigsten Wert oder ca. 68 % des Gewichtes der Schilddrüse beim Neugeborenen im Alter von 2—3 Monaten. Von diesem Alter an beginnt das Gewicht wieder langsam zuzunehmen.

3) Bei frühgeborenen Kindern verhält es sich entsprechend, nur sind die absoluten Gewichte bedeutend niedriger, da, wie gleichfalls aus diesem Material hervorgeht, die Schilddrüse gegen das Ende der Schwangerschaft stark zunimmt.

4) Ein Unterschied in der Grösse der Schilddrüse zwischen den Geschlechtern ist nicht nachweisbar.

5) Kongenitale Struma wurde bei 10 Patienten des Materials, d. h. in 6,25 % gefunden. Bei prämaturen Kindern wurde kein einziger Fall von Struma angetroffen.

6) Es lässt sich nicht nachweisen, dass Dauer und Art der Krankheit die absoluten Gewichte der Schilddrüse beeinflussen. Andererseits scheint die Grösse der Schilddrüse, berechnet in Prozent des Durchschnittsgewichtes für dasselbe Alter, mit der Krankheitsdauer abzunehmen.

Sobre el peso del tiroides en los niños de 0—2 años.

1) En 244 niños de edad comprendida entre 0—2 años muertos de enfermedades diversas se estudió el peso del tiroides.

2) Los resultados muestran que el peso absoluto del tiroides es constante y aproximadamente de 3 gramos durante todo el primer mes de la vida. Posteriormente el peso desciende alcanzando su valor mínimo de alrededor de un 68 % del peso del tiroides en el momento del nacimiento a la edad de 2—3 meses. A partir de esta época nuevamente empieza a aumentar el peso lentamente.

3) Lo propio ocurre en los prematuros en los cuales el peso absoluto es considerablemente mas bajo, desprendiéndose de ello como hecho evidente que el tiroides aumenta considerablemente hacia el final del embarazo.

4) No pudieron encontrarse diferencias en cuanto al tamaño del tiroides en los dos sexos.

5) En 10 casos se encontró un bocio congénito, o sea, en una proporción del 6,25 %. En los prematuros no se halló ni un solo caso de bocio.

6) La duración y el tipo de enfermedad no puede ser demostrativa sobre el efecto en relación al peso absoluto del tiroides, por otra parte el tamaño de dicha glandula calculado como un porcentaje del peso medio para la misma edad parece disminuir al prolongarse la duración de la enfermedad.

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FROM THE SACHS' HOSPITAL FOR CHILDREN AND THE SWEDISH PUBLIC HEALTH INSTITUTE.

Airborne Infections

VI. Continued investigations into the control of dustborne streptococcal infections in infants' wards

by

GUNNAR LAURELL

One of the methods that has been widely applied in practice to control dust- and airborne infections is the oiling of floors and textiles. The results, which have been reported by many investigators (2, 5, 10, 11, 12, 13) have varied. In Sweden, the method was tried out at the Sachs' Hospital for Children in Stockholm during the years 1946—47. The number of nosocomial infections were higher in the wards treated with oil than in the control ward, and dust-suppressive measures failed to prevent extensive streptococcal contamination of the ward. The investigation was extended to include the autumn of 1947 and the spring of 1948 and the result of these continued studies will be presented in this paper.

Scope of the investigation

The period covered by the investigation extended from Nov. 17, 1947, to May 15, 1948, and as in the previous study, the experiments were conducted at the Sachs' Hospital for Children. In one ward the floors and textiles were treated with oil and another identical ward was used as a control.

The distribution of the patients over various age-classes will be seen in figure 1.

The majority of the patients were infants and children of up to 3 years of age, and to a certain extent, up to the age of 6—7 years. A

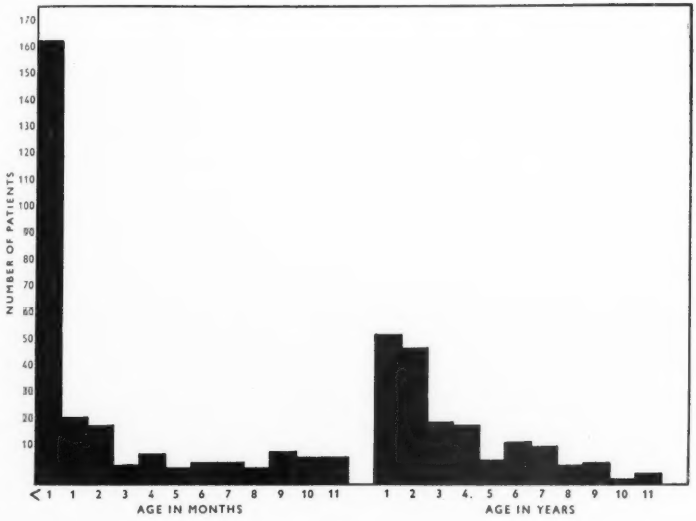

Fig. 1.

feature of interest was that among the 292 patients under 1 year of age 75 had been born before term. The material can be regarded as a representative sample of the patients at a children's hospital.

Methods

The plan of the hospital wards, the routine methods employed at the hospital for controlling infection, and the technique of the clinical and bacteriologic examinations have been described in earlier publications (3, 4, 5). The bacteriologic analyses were mainly directed to the beta hemolytic streptococci. The serologic typing of the streptococcal strains isolated was done by Dr. P. HEDLUND at The State Bacteriologic Laboratory. Nose and throat cultures were taken from the patients once a day during the first three days of their hospital stay, and subsequently twice a week. In all, 6926 specimens were examined. From the hospital staff nose and throat cultures were obtained when they began service and after that twice a week. In all, 2688 specimens were examined. All patients infected with hemolytic streptococci were examined by the so-called "spreading test". The floors and textiles were oiled in the same way as in the preceding investigation.

Table 1.

Method	Experimental material	Number	Streptococcal Infections			
			No nosocomial infection		Nosocomial infection	
			No.	Percentage	No.	Percentage
Oiled	Patients	256	13	5.0	6	2.4
unit	Staff	48	5	10.0	6	12.5
Unoiled	Patients	252	16	6.3	7	2.8
unit	Staff	41	5	12.0	6	15.0

Occurrence of streptococci in patients

The occurrence of hemolytic streptococci in patients and hospital staff will be seen in table 1.

Ward I (Control unit). Of 252 children, 23 had hemolytic streptococci in the nose or throat. Among these 23 children, 16 were found to harbour streptococci at the time of admission and 7 became infected while at the hospital. If a case is to be regarded as a nosocomial infection, two negative cultures must precede the first positive culture. These 7 children, 2.8 per cent, thus constituted the number of nosocomial streptococcal infections. The majority of the strains isolated were typed and untypable strains alone were found in two children only. Group A was represented by types 1, 6, 9, 12 and 25. Strains belonging to group C were encountered remarkably often, namely, in 6 children, 4 of whom had contracted the infection at the hospital. In one child with only one positive sample, the strains belonged to groups G and B. Two strains belonged to group B, one strain to group F and one to group L. The strain belonging to group F was isolated in a child admitted on account of an infection that was considered, on the basis of the clinical findings, to be a streptococcal infection. Strains belonging to type A 18 were also found in this child.

Ward II (Oiled unit). Hemolytic streptococci were isolated in 19 of the 256 children in this ward. Among these, streptococci were found in 13 at the time of admission and 6 became infected

at the hospital. Thus, the incidence of nosocomial infections in this ward was 2.4 per cent. Not in a single child could untypable strains alone be demonstrated. The strains in group A belonged to types 1, 6, 19 and 28. As in the control ward, strains from group C were common, being demostrated in 7 children. Two of these children contracted the infection at the hospital. In 4 children the strains belonged to group G. Two children were carriers of strains belonging to group K, and one of strains from group E.

Occurrence of streptococci in medical staff

Streptococci were isolated from 2 of the 7 physicians serving in the wards in both instances at the time when they began their service. Later on one of these two physicians became infected again, while at the hospital, with strains belonging to group C and in connection with this infection was a carrier of streptococci belonging to this group for three weeks. None of the physicians was proved to be a dangerous carrier, and in no case was it found that any of the physicians caused secondary infection in the children.

Occurrence of streptococci in hospital staff

Control ward. In this ward there were 41 nurses and wet nurses. Hemolytic streptococci were demonstrated in 9 of them. Five were infected when they started service and two of these later contracted an infection at the hospital. Four other nurses became infected while at the hospital. The strains isolated from the nurses who contracted the infection at the hospital belonged to group C in 3 instances and to group G in one. The strains isolated from 2 nurses could not be typed. None of the staff proved to be a dangerous carrier.

Oiled ward. Forty-eight nurses were serving in this ward. Streptococci were isolated from 7 of them. Five were infected when they began their service but all of these were re-infected while serving at the hospital. Two other nurses contracted the

infection at the hospital. In the nosocomial cases, the strains belonged to group C in five instances; two strains were untypable. The streptococci were isolated from the throat alone in every instance, and none of the staff proved to be a dangerous carrier. On no occasion was it proved that the hospital staff were the cause of secondary cases.

Clinical signs

The majority of the children had only a mild form of infection and 11 children were merely healthy carriers. The most common clinical signs and symptoms may be described in the following way:

Type of infection. The majority of infections were described as pharyngitis, rhinopharyngitis, tonsillitis and infected adenoids. One child had been hospitalized for eczema pustulosa varicelliformis Kaposi (1). Hemolytic streptococci were demonstrated in this child after culturing from pus blisters. Another child was admitted as a skin case, with streptococci in an infected herpes simplex of the face. One child was hospitalized for acute dyspepsia, and streptococci were isolated during the acute stage in the stools. One child who had been ill fourteen days before hospitalization with a throat infection was admitted suffering from glomerulonephritis. An interesting feature in connection with the result of the serologic typing was that 6 of the children with streptococci belonging to group C had clinically established infections. Children harbouring strains from groups E, F, G and K were as a rule healthy carriers or had only mild clinical symptoms. It is also of interest to note that streptococcal infections were not especially common among the patients belonging to the lowest age-class, under 1 year of age. There were 12 cases in this group. In the 1—3 year age-group there were 19 cases, evenly distributed, and the remaining 11 cases occurred as isolated cases in the higher age-groups. Streptococci were isolated from only three of the premature infants and from three of the newborn full-term infants.

Fever. The temperature was often high, 40—41° C during the first few days of illness, but as a rule it did not remain high for more than 3—5 days.

Nose and throat. It was observed at the physical examination that in most patients the throat was red and inflamed with enlarged tonsils and exudation. Enlarged lymph glands were a common finding, and some of the patients had coryza with a purulent discharge.

Laboratory data. The sedimentation rate and white blood cell count were as a rule only slightly increased.

Treatment. In this investigation both clinical cases and healthy carriers were treated with penicillin as soon as possible. The object of this was to prevent nosocomial infections by getting rid of potential spreaders as quickly as possible. As a rule, even after a few days' treatment, streptococci were no longer isolated from the respiratory tract.

Complications were infrequent and glomerulonephritis developed in only one child after a streptococcus infection (case report 332/48).

Staff. The clinical infections were of the same kind as those occurring in the children. The symptoms were mild in most instances, and healthy carriers were common.

Case reports

In order to illustrate the types of infection commonly encountered in this investigation a few typical cases will be described here.

Case 124/48. A newborn male infant was hospitalized because of prematurity. Weight at birth 1340 g. General condition satisfactory on admission. No infections during the first week at the hospital. On the 8th day in hospital the infant began to suffer from moderately severe dyspepsia and had a temperature of up to 38° C for 3—4 days. White blood cell count on 10th day in hospital 16 900. In connection with this infection large numbers of hemolytic streptococci which were typed as belonging to group C, were isolated from the throat. Previous bacteriologic cultures had only demonstrated staphylococcus aureus and coliform bacteria. Penicillin and elkosin (6-sulphanilamido 2-4-dimethylpyramidine) treatment was instituted on the 9th day in hospital and the infection gradually subsided after a few days. The streptococci also disappeared in response to the treatment, and they were not found again during the two months the infant remained at the hospital. This case is fairly typical of the relatively mild nosocomial infections that occurred,

Case 141/48. A girl aged 9 years was admitted for observation because of possible mongolism. Nothing in the personal history indicated that the child had recently had any infection. It was observed at the physical examination that the child had a slight rhinitis but treatment was not considered necessary. Bacteriologic cultures nevertheless contained large numbers of beta hemolytic streptococci, of type 18, in the nose and throat on the day of admission. The spreading test revealed the presence of streptococci on the upper lip, both hands and the night gown. Penicillin therapy was instituted on the third day in hospital in a dose of 20 000 I. U. i. m. 8 times daily, and after two days' treatment streptococci were no longer demonstrable in the respiratory tract.

This is a typical case of a practically healthy spreader of streptococci, hospitalized for some reason other than infection. The routine bacteriologic examination revealed that the patient was a streptococcus spreader. The infection was rapidly cured with penicillin.

Case 75/48. A newborn female infant was admitted because of prematurity. Weight at birth 1880 g. General condition good on admission. During the first six weeks in hospital the infant developed normally. Mild dyspepsia then developed, and lasted for about a week. In connection with this disease, streptococci, belonging to group C were isolated from the throat over a period of four days. Penicillin and elkosin therapy was given. The streptococci disappeared in response to the treatment and the infection subsided. When discharged two weeks later the infant was healthy and free from streptococci.

This is a typical case of a nosocomial infection where the symptoms appeared in connection with the isolation of streptococci of group C from the throat.

Case 332/48. A boy aged 8 years was hospitalized on the suspicion of a kidney disease. Three weeks before his admission he had been ill with fever and a sore throat. His temperature dropped back to normal without any treatment. He was admitted for observation because his urine had been abnormally dark for a few days. The physical examination revealed that his throat was moderately inflamed and that he had a slight rhinitis but there were no other signs of active acute infection. A large number of red blood cells were found in the urine and the Heller test was positive. Nonprotein nitrogen in blood 32 mg %. Antistreptolysin titer 800 units, microsedimentation rate 20 mm. The routine bacteriologic examination revealed large numbers of beta hemolytic streptococci of type A 25 in both nose and throat. In the spreading test, streptococci of the same type were isolated. As the child was therefore presumed to be a spreader, penicillin therapy was instituted on the second day after admission. The following day only a few streptococci were found in the throat and the spreading test was negative. On

the second day of treatment no streptococci were isolated from the nose or throat, and the child was subsequently free from these organisms. The acute kidney symptoms also disappeared rapidly, but the child had not completely recovered when he was discharged three weeks later.

This case is a typical example of an acute streptococcal infection in which the acute symptoms from the respiratory tract had subsided and the condition was dominated by a glomerulonephritis. The bacteriologic examination revealed that the child was a spreader of pathogenic streptococci. The hemolytic streptococci rapidly disappeared after penicillin treatment.

Streptococci in dust

The result of the analyses of dust from the two units will be found in figures 2 and 3. A total of 526 samples from Ward I were examined and 131 were found to contain streptococci; from Ward II, 521 samples were analysed and 84 contained streptococci. As will be seen from the figures, the presence of streptococci was a relatively constant finding in both the oiled and the unoiled wards during certain periods. Free intervals of varying duration also occurred. Quantitatively speaking, the streptococci were present in small numbers; in only a few cases were large numbers observed. As in the case of the 1946—47 investigation large numbers of streptococci were observed only when dangerous carriers were being treated in the wards. In this investigation also as early as 12—18 hours after a spreader had been admitted to a ward, streptococci of the same type as in the affected child were demonstrable in the dust not only in the room where the child was lying, but also in all the other rooms as well as in the corridors and examination rooms. In the unoiled unit, this was demonstrated in connection with the admission of a patient with coryza with a purulent discharge. In the oiled ward, the same occurrence was noted when a child suffering from an infected herpes simplex was admitted. The result of the serologic typing of the hemolytic streptococci in the dust is shown in table 2.

As a rule the types found in the dust were the same as those found in both staff and patients. The dust analysis thus in large part reflected the occurrence of streptococci in patients and staff.

Dept. I

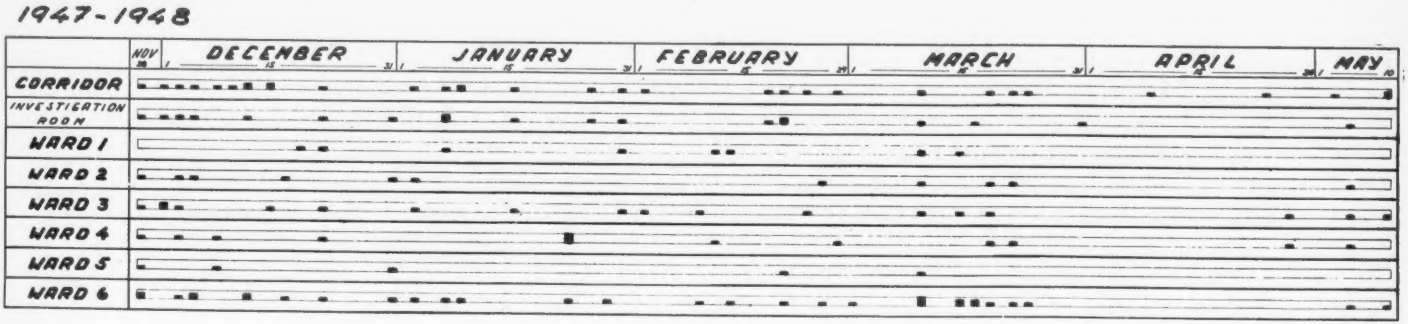

Fig. 2. Diagram showing occurrence of beta hemolytic streptococci in hospital for children. Bacterial content of dust (sparse, moderate, abundant) evident from height of respective black columns.

Dept. II

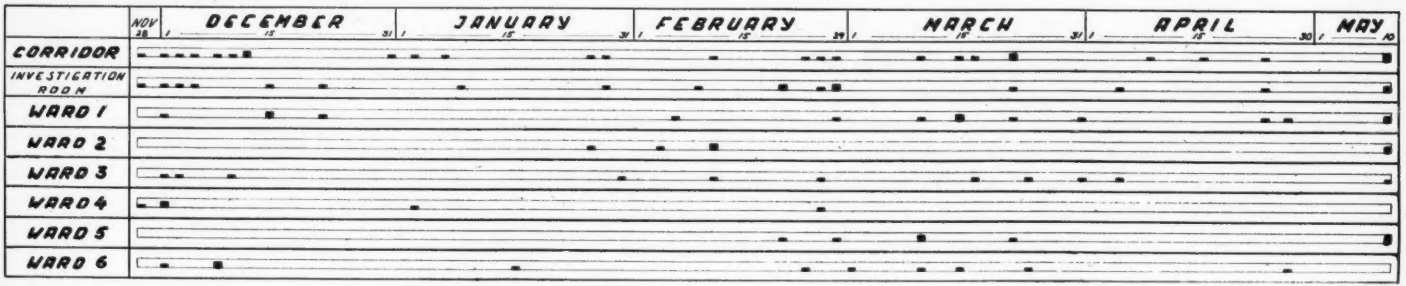

Fig. 3. For explanation of signs see fig. 2.

Table 2.

Groups and types of streptococci isolated from dust.

Type or group	Number of strains	
	Dept. I	Dept. II
A1	1	1
A6	26	13
A12	4	5
A15	2	1
A18	1	2
A19	5	3
Typable group A strains	39	25
C	69	43
B	11	11
E	3	2
D	2	0
K	2	1
F	0	2
G	0	4
Untypable	4	3

Fig. 3. For explanation of signs see fig. 2.

Streptococci in the air

Ordinary sedimentation plates were used for demonstrating the presence of streptococci in the air. The air was not consistently examined in all rooms but for the most part only in rooms where infected patients were lying and in the corridors connecting the rooms. In Ward I, 653 samples were analysed and among these 32 were found to contain streptococci; in Ward II 638 samples were studied and 14 contained streptococci. The positive sedimentation plates were found at fairly regularly spaced intervals during the period covered by the investigation. Only during one period from the end of February to the middle of March were a large number of positive plates obtained from one of the rooms in Ward I. The strains were for the most part of types 6 or 12 in Lancefield's group A. This accumulation of positive plates was

probably due to the fact that two spreaders, one belonging to type 6 and the other to type 12, were under treatment in the ward at that time. The serologic typing otherwise displayed good agreement with that shown in the dust. As in the case of the dust analyses when a spreader was present in a ward, streptococci of the same type were found in the air.

Discussion

The investigations into the effectiveness of the method of oiling floors and textiles for controlling dust and airborne infections were continued at the Sachs' Hospital for Children during the autumn of 1947 and the spring of 1948. This study was mainly concerned with infections due to hemolytic streptococci. The result obtained was that the number of nosocomial infections in the oiled ward was 2.4 per cent while in the control ward it was 2.8 per cent. Among the staff, the corresponding figures were 12.5 per cent and 15 per cent respectively. There was thus no difference between the two departments, a finding that coincides with the result of the 1946—47 investigation. Accordingly this investigation also failed to produce any evidence in favour of oil treatment. This tallies with the view now expressed in Anglo-saxon publications (6, 7, 8, 9). The following conclusion may be cited from an article in the American Journal of Public Health from 1949. "On the whole it appears that dust control alone will not prove to be of great value as a general method of control of airborne disease".

In passing judgment it should, however, be borne in mind that the low incidence of streptococci in this investigation has in general rendered it difficult to estimate the value of the oiling method. Both the primary and the nosocomial infections have for the most part been of a mild nature and healthy carriers were common. A feature of some interest was that the infections were not all caused by streptococci of Lancefield's group A. Clinically established infections due to streptococci of group C also occurred. If the strains belonged to groups E, F, G and K they had usually been isolated from healthy carriers or in connec-

tion with infections that were uncertain, clinically. An interesting observation was that streptococcal infections were comparatively uncommon among the patients in the lowest age groups, especially in the premature and newborn, full-term groups.

Certain details that came out in connection with the investigation have, however, thrown light on the value of the oil method. In dust and air analysis, streptococci were constantly found in certain periods while the intervening periods were free from these organisms. Streptococci were found in particularly large numbers during the periods when so-called dangerous carriers were in the wards. As early as 12—24 hours after the carriers had been admitted streptcocci were found in both air and dust, and they spread rapidly through the ward. This was noted in both units, and oiling did not prevent this spread. The fact that streptococci, over long periods, were often isolated from the dust demonstrates that dust must still be regarded as a source of infection. The part played by contaminated dust in spreading infections is not yet clear.

The routine bacteriologic tests proved to be of great value. Thanks to the fact that dangerous carriers were detected at an early stage treatment could be instituted almost at once. Penicillin was used with success. It seems possible that treatment of carriers with penicillin was a contributory factor in keeping the incidence of nosocomial infections relatively low in this investigation.

Summary

Continued investigations into the effectiveness of oiling floors and textiles in the control of air- and dustborne infections gave a negative result. No difference in the incidence of nosocomial streptococcal infections was noted in a ward treated with oil as compared with a ward that had not been treated. The incidence of streptococcal infections was, however, in general low.

Infections dues aux substances transportées par l'air. VI. Nouvelles expériences concernant le controle des infections streptococciques dans les hôpitaux d'enfants diffusées par les poussières de l'air.

Les nouvelles expériences poursuivies pour rechercher l'effet obtenu en huilant les planchers et les matières textiles du point de vue des infections transmises par l'air et les poussières qu'il transporte ont donné un résultat négatif. On ne constata aucune difference vis à vis de ces infections streptococciques nosocomiales que le service ait été traitée par l'huile ou non. Dans les deux cas, ces infections étaient quoi qu'il en soit faibles, en général.

Infektionen, welche durch die Luft übertragen werden. VI. Forsetzung der Forschungen über die Bekämpfung der durch Staub übertragenen Streptokokkeninfektionen in Säuglingsabteilungen.

Eine Fortsetzung der Forschungen über die Wirksamkeit einer Ölung von Fussböden und Webwaren bei der Bekämpfung von Infektionen, welche durch Luft und Staub übertragen werden, ergab ein negatives Resultat. Bei dem Vergleich einer Abteilung, wo man Öl angewendet hatte, mit einer solchen, wo keines gebraucht worden war, wurde kein Unterschied im Vorkommen von Streptokokkeninfektionen der Nase festgestellt. Das Vorkommen von Streptokokkeninfektionen war jedoch im allgemeinen selten.

Infecciones aereas. VI. Investigaciones sobre el control de las infecciones por estreptococos contenidos en el polvo de las guarderías infantiles.

Las investigaciones concernientes sobre la capacidad protectora de los suelos encerados y textiles en la prevención de las infecciones transmitidas por el aire y polvo han producido resultados negativos; no se han encontrado diferencias evidentes en la incidencia de infecciones estreptococicas nosocomiales entre las guarderías en que se habían o no tomado estas medidas de precaución. La frecuencia de estas infecciones estreptococicas era sin embargo en general baja.

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CLINIQUE ET POLICLINIQUE DES MALADIES DE L'ENFANCE. — UNIVERSITÉ DE LIÈGE. (PROF. A. LAMBRECHTS.)

Iron Metabolism in Infants

I. The Intake of Iron in Breast Feeding and Artificial Feeding (Milk and Milk Foods)

by

Y. M. FEUILLEN and **M. PLUMIER**

As a part of our investigations on the metabolism of iron in infants, the object of these first experiments has been to establish the quantities of iron ingested respectively by children breast fed, fed with pooled human milk and fed artificially.

The figures given in the literature, relating to this subject, are numerous but not very conclusive. Suffice it to quote, amongst others, the results obtained by several authors on breast milk, as follows:

LESNÉ, CLEMENT, ZIZINE (5)	1930;	0.92 mg/l (0.75—1.15)
WALLGREN (9)	1932;	0.43 mg/l (0.22—1.05)
ALBERS (1)	1941;	1.50 mg/l

Similarly for cow's milk:

LESNÉ, CLÉMENT, ZIZINE (5).	1930;	0.92 mg/l
WALLGREN (9)	1932;	0.85—1.11 mg/l
KRAUSS, WASHBURN (3)	1936;	0.36—0.53 mg/l
ALBERS (1)	1941;	0.75 mg/l

There are great variations between these results, which can supposedly be explained by use of different analytical technics, often insufficiently accurate, and also by the lack of sufficient precautions when taking samples.

In view of these contradictory results, we have restudied this question whilst taking all necessary precautions. The question is indeed of great importance. The problem is to *discover if*, as certain authors suppose, *anemia in artificially fed infants is due to the fact that cow's milk is very poor in iron.*

Method

Acid soluble iron.

For estimating the iron in cow's milk we have used the O-phenanthrolin colorimetric method after HEILMEYER and PLÖTNER (2) for plasma iron: addition of HCl, precipitation of proteins by trichloracetic acid, reduction to ferrous iron and coloration by O-phenanthrolin. Since certain factors (pH, acid anion) influence the time for development of the coloured complex, as shown previously by VAHLQUIST (8) and by one of us (6), it is as well to wait 24 hours before taking the colorimetric reading.

For breast milk, since the precipitation of the proteins by HCl and trichloracetic acid is much less complete (production of much finer lumps), we found that the precipitation improved when it took place on a water-bath at 60° C for 10 minutes.

Total iron.

Estimation by the same colorimetric method after sulphuric-perchloric acid digestion.

N. B. None of the estimations was considered of value unless the duplicates were good.

Results

A) *Breast milk*, taken from the breast in the middle of sucking.

N°	Time of lactation	Total iron (γ %)
1	3 weeks	35
2	1 month	70
3	2 months	20
4	2 "	80
5	2 "	41
6	2 "	71
7	4 "	39
8	4 "	49
9	6 "	65
10	8 "	40
		Mean: 50

B) *Pooled Breast milk*, from the Lactarium, Liège.

Number of samples .... 40 (from 36 different mothers)
Mean..... 58 γ%
Variations ..... 27—121 γ%

C) *Breast milk*, comparative *variations with the time of lactation.*

Time of lactation	Number of data	Means
15 days—2 months	9	60 γ%
3—5 months	11	60 γ%
6—7 "	9	54 γ%

D) *Breast milk:* Comparison between the estimation of *acid soluble and total iron.*

Acid soluble iron	Total iron
25	27
85	85
75	85
69	61
76	81
47	50
107	103
69 γ%	70 γ%

E) *Cow's milk taken directly from the udder* in a beaker washed with double distilled water.

	Acid soluble iron	Total iron
	23	25
	38	44
	82	75
	40	35
Mean:	45 γ%	44.8 γ%

F) *Dairy milk, bottled* or distributed by the *jug.*

Bottled (7 samples)
Jug (4 samples)
Mean: 122 γ%; Variations: 68—185 γ%.

G) *Different diets* given at the Clinique des Maladies de l'Enfance.

Diets	Number of samples	Means (γ %)	Variations
Mixture 2/3 milk, 1/3 water, 5 % saccharose, 3 % starch	77	135	62—310
Butter milk (prepared by the Clinic)	20	490	180—735
Butter milk Eledon Nestlé 10 % + 5 % Nutromalt Wander	29	176	75—272
Acid milk (prepared by the Clinic).	35	212	120—565
Pelargon Nestlé 20 %	19	236	190—365
Tinned vegetable soup.....	9	63 γ/g dried	43—92
Fresh " "	38	131 γ/g dried	80—206

Discussion

A) *Breast milk.*

Our estimations of iron in breast milk showed very little difference (about 10 γ%) between milk taken directly from the breast and that provided by a milk bank. This difference is due to the manipulation to which the milk is subjected at the Lactarium, as metal recipients are not employed.

Similarly to WALLGREN, we found no difference in the quantities of iron present in the milk taken at different periods of the lactation (9).

Confirming the work of STARKENSTEIN and WEDEN (7), we found that all the iron in the milk is acid soluble: the results of estimations of soluble iron and total iron were identical within the limits of experimental error.

Altogether, our results show that the excretion of iron in milk is little, about 0.5 mg/liter, which represents a negligible loss to the maternal organism.

It is to be noted that our results are similar to those of WALLGREN (9) who gives a mean value of 0.43 mg/liter, but deviate from those of ALBERS (1) who finds 1.5 mg/liter. Thus we were able to observe that the method used by ALBERS (method of Heilmeyer and Plötner) produces a slightly cloudy filtrate in breast milk, which artificially increases the extinction coefficient. Hence the necessity (see above) in practice of heating during the precipitation of the proteins.

B) *Cow's milk from the udder.*

Our results resemble those of KRAUSS and WASHBURN (3): 0.36—0.53 mg/l; but we cannot agree with the results of ALBERS who finds great differences between cow's milk and breast milk, in favor of the latter.

Our first estimations for cow's milk taken directly from the udder allow us to eliminate it as the principal cause of anemia in infants fed artificially since there is a relatively small difference between the iron in breast and cow's milk.

C) *Diets given in the Clinic.*

This view is further supported by the following results: It is known (LANGSTEIN (4), WALLGREN (9)) that milk can be enriched in iron by its passage in metal recipients. It seemed interesting to us to estimate the iron not only in milk taken directly from the udder, but also commercially prepared as received and consumed by infants. The greatly increased values that we thus obtained (122 γ%) were explained by the preparation and transport in metal recipients; there was either formation of iron lactate (lactic acid + iron hydroxide of the iron recipients) or accidental addition of rust.

As infants are not fed entirely by milk, we have estimated the quantities of iron present in diets most frequently employed in pediatric clinics. The mixture of milk, diluted 1/3, to which is added 5% saccharose + 3% of flour sifted at 72% gives us a slightly higher result (135 γ%) than milk alone, which can be explained by the manipulations and the presence of the iron in the flour (about 1 mg%). The quantity of iron found in butter milk prepared by the diet kitchen of our Clinic was extremely high. This is in relation to the method of preparation which includes passing through an iron sieve. The results we obtained for the estimations in butter milk Eledon Nestlé, acid milk and Pélargon Nestlé were equally high: these increased quantities are due to the lactic acid in their preparation, which dissolves the iron hydroxide of the recipients. Finally we mention the quantities of iron we found in vegetable soup (fresh and tinned) which we generally add to the diet of infants past three months of age.

In view of these results we can conclude that *anemia in infants fed artificially is not due to the lack of iron in their diet.* In fact these infants often ingest 3 to 4 times more iron than infants of the same age breast fed. We intend to examine in a future work the extent to which the supplementary iron is absorbed by the intestine of the infant.

We wish to express our best thanks to Miss N. Billerey for her excellent technical assistance.

Summary

In this first part of their investigations on iron metabolism in infants, the authors have estimated the iron in breast milk, cow's milk and different diets most frequently employed in pediatric clinics. They conclude that infants fed artificially often ingest 3 to 4 times more iron than infants of the same age, breast fed; and that anemia in the former is not due to the lack of iron in their diet.

Le métabolisme du fer chez le nourrisson. 1. L'ingestion du fer chez les enfants nourris au sein et nourris artificiellement.

Dans cette première partie de leurs recherches sur le métabolisme du fer chez le nourrisson, les auteurs ont dosé le fer dans le lait de femme, le lait de vache, et différents régimes habituellement employés en clinique infantile. Ils en concluent que les enfants nourris artificiellement ingèrent fréquemment jusqu'à 3 et 4 fois autant de fer que les enfants nourris au sein. L'anémie des nourrissons soumis au régime artificiel n'est donc pas due au manque de fer dans leur alimentation.

Eisenstoffwechsel bei Säuglingen. 1. Das Einnehmen des Eisens von Brustkinder und Flaschenkinder.

Im ersten Teile dieser Untersuchungen über Eisenstoffwechsel bei Säuglingen, wurde die Menge Eisen festgestellt, die in Brustmilch, Kuhmilch und den verschiedenen, am häufigsten in Kinderkliniken angewendeten Diäten enthalten ist. Man schliesst daraus, dass Flaschenkinder oft bis zu 3 oder 4 Mal mehr Eisen als Brustkinder zu sich nehmen, und dass Anämie bei den ersteren nicht einem Mangel an Eisen in deren Ernährung zuzuschreiben ist.

Metabolismo del hierro en la infancia. 1. Cantidades de hierro en la lactancia materna y en la lactancia artificial (Leche y productos lácteos).

En la primera parte de sus investigaciones sobre el metabolismo del hierro en la infancia los autores han determinado las tasas de hierro existentes en la leche de mujer, leche de vaca y en las diferentes dietas que más frecuentemente se emplean en las clínicas de pediatría. Llegan a la conclusión que los niños que siguen lactancia artificial frecuentemente ingieren de 3 a 4 veces mas hierro que los niños de la misma edad alimentados con lactancia materna, por lo tanto la anemia en los primeros no es debida a una falta de hierro en su dieta.

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ACTH in the Treatment of Juvenile Rheumatoid Arthritis[1]

by

J. VESTERDAL, O. REMVIG and M. SPRECHLER

Only a few reports on ACTH treatment in juvenile rheumatoid arthritis have appeared till now. ASTRUP et al. have published one case, and FREYBERG et al. have mentioned two cases.

On the other hand, a rather large number of cases of the adult form of rheumatoid arthritis treated with ACTH have been published after the first report of HENCH et al. The reader is referred to the survey of THORN et al. It is now the general opinion that the improvement, sometimes dramatic, which starts a few hours after the first injection of ACTH, in most cases is followed by a relapse when the drug is withdrawn, and that the therapy cannot be maintained in sufficiently large doses for a long time because of the risk of endocrine side-effects. This differs from the experiences with acute rheumatic fever, where the effect often seems to be long-lasting or even permanent.

Juvenile rheumatoid arthritis, however, differs from the adult form in various respects. From a series of about 150 cases SURY draws the following conclusions: In some of the cases the disease runs a mild course and subsides without leaving any serious invalidity. A great part, about half of the cases, are severe, characterized by great activity of the joint involvement, often with periods of high irregular fever, and sometimes swelling of the spleen and lymph nodes occurs. There is a considerable tendency

[1] A preliminary report was read to the Danish Pediatric Society May 20th, 1951.

to development of deformities which after a few weeks may become quite intractable. In these cases early invalidity is the result. Eye complications (chronic iridocyclitis, often combined with bandshaped corneal opacity) may occur. These were found in 21 per cent of the cases by E. VESTERDAL et B. SURY. In the adult form, eye complications are rare, except in spondylarthritis, and generally consist in recurrent attacks of acute iritis or scleritis without bandshaped corneal opacity.

Owing to these differences we have thought it worth while to try whether or not ACTH has a better effect in the juvenile than in the adult form. In cases with developing deformities we have considered ACTH to be indicated, in the hope that the deformities would be corrected with the disappearance of joint stiffness during the treatment.

Case material

We have treated 7 cases with a total of 10 treatment series. The relevant facts of these cases are summarized in table 1. Some of the patients (nos. 1, 2, 3, and 5) had received gold therapy earlier. They had all received physical therapy before, and this was continued during the ACTH treatment.

The disease was in different stages in these cases, indicated in the table according to the classification of the American Rheumatoid Association (class I: Complete functional capacity with ability to carry out all usual duties without handicap; class II: Functional capacity adequate to conduct normal activities despite handicap of discomfort or limited mobility of one or more joints; class III: Functional capacity adequate to perform only little or none of the duties of usual occupation or self-care, class IV: Largely or wholly incapacitated with patient bedridden or confined to wheel-chair, permitting little or no self-care).

In addition, the degree of activity of the disease is noted in the table. Naturally, this can only be roughly estimated by appraisal of the tenderness and swelling of the joints, the progression of deformities, the occurrence of fever and increased sedimentation rate. The sedimentation rate alone is insufficient for estimation of the activity, as it may be rather high without other signs of activity. Thus in our case no. 4 the sedimentation rate was 81 mm/1 hr., with only slight activity otherwise.

None of our patients had eye complications, splenomegaly or enlarged lymph nodes.

Table 1.

Case no.	Sex	Age (yrs)	Duration of illness prior to treatment (years)	Stage	Degree of activity	Dosage of ACTH		Effect of ACTH on:							Relapse
						total (mg)	days	Tenderness	Mobility	Capsular swelling	Deformities	Eosinophil response	Sedimentation rate (mm) Before treatm.	Sedimentation rate (mm) Lowest value during treatm.	
1. (2/51)	M.	12	3	IV	++	418	19	+	+	+	0	+	85	43	Two days before discontin. of treatment.
2. (84/50	F.	10	2	III	+++	166	12	+	0	0	0	+	60	10	At discontinuance of treatment.
3. (578/50)	F.	9	$1^1/_2$	III	++	288	11	(+)	0	0	0	?[1]	51	17	After 2 days, except for deformities, where effect was lasting.
					++	244	14	+	++	+	+	?[1]	43	21	
					++	555	37	+	+	+		?[1]	70	14	2 weeks before discontinuance of treatment.
4. (103/51)	F.	12	3	II	+	252	11	+	+	0	+	0	81	75	Therapy discontinued because of fever.
5. (793/50)	F.	9	7	II	++	270	13	+	+	0	+	+	20	7	Moderate relapse 2 wks after discont. of therapy.
6. (473/51)	F.	$2^1/_2$	$1^1/_2$	II	++	192	10	+	+	+	0	0	25	16	1 week later.
					++	360	21	+	+	+	0	0	21[2]	21[2]	2 days before discont. of therapy.
7. (937/50)	M.	7	3	III	+++	404	34	++	++	+	++	+	135	9	No relapse (observation time $3^1/_2$ mos.).

[1] Eosinophil count almost zero prior to treatment.

[2] Micro-technique.

Treatment

The question of dosage of ACTH in children has not been settled by previous authors. FREYBERG *et al.* are of the opinion that children require the same dosage as do adults, but they have treated only two cases. In our experience, the dosage may be reduced somewhat in children though not in proportion to weight, but rather in proportion to surface area. Further studies in this field are being carried out.

We have administered 24 international units of ACTH daily, divided into 4 intramuscular injections with 6-hour intervals, and in most cases this seems to have been an adequate dosage, both clinically and as measured by the urinary excretion of adrenocortical hormones. On two occasions (case 3, 1st series, and case 4) the effect, however, was only poor. With regard to the first of these, the ACTH preparation employed proved to be almost ineffective in the experience of other investigators, as well. In all the other series another preparation ("Acton", Fredriksberg Chemical Factories, Inc.) was used.[1] The other patient mentioned above (case 4), in whom 24 I. U. daily had only a poor effect, is at present under treatment with 60 I.U. daily (divided into four doses) with another batch of "Acton", but with only slightly better effect. This is thought to be due to the low activity of her arthritis.

A dosage of 24 I. U. daily was in most cases maintained for 6—14 days and then tapered slowly, in some cases with reduction of the number of injections to 3 per day. Most of the children were treated in periods of 2—3 weeks; only two periods were longer (case 3, 3rd series, and case 7).

After encountering two cases of low serum potassium during ACTH treatment (see later) we gave a daily supply of 0.2—0.3 g potassium ion as a solution of primary and secondary phosphate, and later on no such side-effects were encountered.

Some authors (MASSELL *et al.*, and others) claim that large doses of ascorbic acid have a favourable effect in rheumatoid arthritis. In order to study this we have in some of the cases (case 3: 3rd series, case 4 and 5, case 6: 2nd series, and case 7) given ascorbic acid, 5 g daily by mouth, in addition to the ACTH treatment; in most cases this was given for a period of 5 days starting 5 days after the beginnning of the ACTH treatment. On some occasions (case 3: 3rd series, case 4, 5, and 7) cholesterol, too, was added, in doses of 1—1.5 g daily by mouth. Details about the administration of these substances have not been listed in the table, as they had no clinical effect, They will be mentioned later.

The physical therapy was continued during the ACTH treatment, particular stress being laid upon correction of deformities.

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[1] The preparation was standardized by Dr. Hamburger, the Hormone Department of the State Serum Institute.

For estimation of the effect the following examinations were carried out: The joints were examined as to deformities, mobility and capsular swelling; the sedimentation rate was determined once or twice a week, and the number of circulating eosinophils were counted daily. For practical reasons this was done 6 hours after the previous ACTH injection. A 4-hour interval would possibly have given lower results.

In some of the cases (case 1, case 3: 3rd series, case 4, 5, and 7) the daily urinary output of 17-ketosteroids (17 ks.) was determined (by the method of HAMBURGER and RASCH), and the corticoids in the urine were determined according to SPRECHLER.

Results

First it must be said that the ascorbic acid and cholesterol had no demonstrable clinical effect. Cholesterol did not influence the hormone excretion, but the ascorbic acid caused a slight decrease in the output of corticoids followed by a slight rise. Further studies on this subject will be published later.

From a clinical point of view, the ascorbic acid and cholesterol may therefore be disregarded, and we will confine our discussion mainly to the ACTH treatment.

The effect of the treatment will appear from table 1, where the results of the examinations are summarized. We add a few comments to each case:

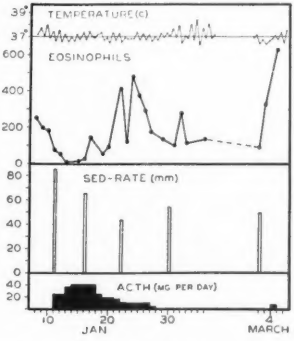

Fig. 1. Case 1. Temperature, eosinophils per c.mm, and sedimentation rate during the treatment. Urticarial reaction to the ACTH injection on March 4th.

Case 1. (Fig. 1). Moderate improvement was seen, though not with regard to the deformities which proved to be due to osseous ankyloses. The symptoms reappeared as soon as the ACTH dosage was reduced. Five weeks later a new series of ACTH injections was started, but after the first injection (6 I.U.) there was a pronounced urticarial eruption, and the treatment was discontinued. Skin tests with swine serum, pork, and the ACTH preparation employed were negative, and so was the Prausnitz-Küstner test with ACTH. The excretion of adrenocortical hormones was not estimated during the first treatment period; prior to the last injection the excretion of corticoid amounted to 0.29 mg/24 hrs., but decreased to 0.08 mg/24 hrs on the day of this injection, whereas the output of 17-ks. did not change.

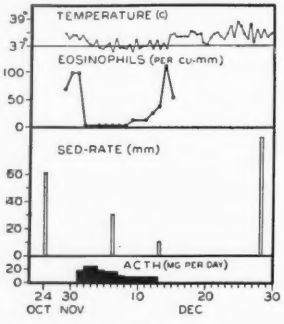

Fig. 2. Case 2. Temperature, eosinophils and sedimentation rate during the treatment.

Case 2. Practically no effect on the joints was seen, in spite of normalisation of the sedimentation rate and disappearence of the circulating eosinophils (Fig. 2).

Case 3. In this patient the number of circulating eosinophils could not be used as a measure of response, as even without treatment, she constantly had an eosinophil count below 25 per c. mm.

She was treated with 3 series of injections. In the first period, 24 I. U. daily had no effect, the ACTH preparation being ineffective, as mentioned before. An increase of the dosage to 60 I. U. daily had only slight effect. Six weeks later she was again treated with ACTH, now with the preparation "Acton", and this had a favorable effect on the joints, including the deformities. Two days after withdrawal of ACTH the symptoms recurred, except for the deformities, on which the effect

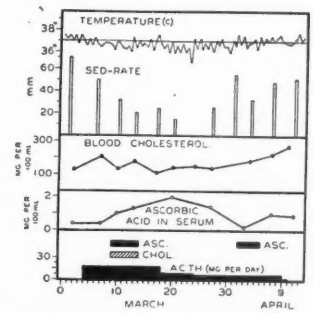

Fig. 3. Case 3. Temperature, sedimentation rate, blood cholesterol, and ascorbic acid in serum during the treatment. The eosinophil count is not indicated, as it was approximately zero prior to, and during the treatment. *Asc.:* ascorbic acid, 5 g daily per mouth. *Chol.:* cholesterol, 1 g daily per mouth.

was lasting. ACTH was again administered six weeks later, this time for a period of 37 days, the dosage after about 2 weeks being reduced to 9 I. U. daily, divided into 3 injections. Ascorbic acid was given during two short periods, and cholesterol was added in the last of these (Fig. 3). Apparently this did not influence the course of the disease; in particular no convincing enhancement of the ACTH effect was seen. During the first part of this period, when the dosage was 24 I. U. daily, the sedimentation rate decreased to normal values, and a beneficial effect on the joints was observed. On reduction of the dosage the symptoms recurred, and the sedimentation rate rose to approximately the same value as prior to treatment. The hormone excretion was examined prior to, and during, the third series of injections. The pre-treatment excretion of corticoids averaged 0.64 mg/24 hrs., and that of the 17-ks. averaged 1.0 mg/24 hrs. A moderate response to ACTH was seen, as the corticoids averaged 0.82 and the 17-ks. averaged 2.6 mg/24 hrs. during the treatment. When the dosage was reduced to 9 I. U. daily, the steroid excretion decreased to values below the pretreatment level.

Case 4. As mentioned above, no effect of the treatment was seen, probably because of the slight degree of activity of her arthritis. The treatment was discontinued, because of fever (38°.9 C.), probably due to infiltrations on the sites of injections. She was treated with penicillin, and the fever subsided after two days. No other signs of infection were found. The corticoids rose from 0.29 mg/24 hrs. before treatment, to an average level of 1.80 mg/24 hrs., and the 17-ks. increased from 2.7 to 5.8 mg/24 hrs. The first day of fever the corticoids reached a value as high as 6.00 mg/24 hrs.

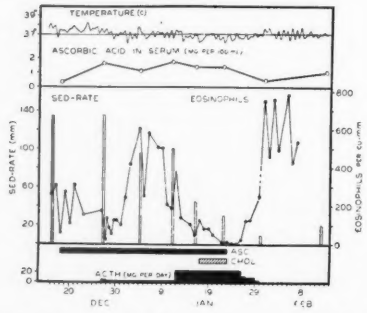

Fig. 4. Case 4. Temperature, ascorbic acid in serum, sedimentation rate, and eosinophils during the treatment. *Asc.*: ascorbic acid, 5g daily per mouth. *Chol.*: cholesterol, 1 g daily per mouth.

Case 5. Moderate effect on the mobility and the deformities was seen. Two weeks after withdrawal of ACTH most of the symptoms reappeared, but the deformities did not recur. The sites of injection were infiltrated and sensitive. Prior to treatment the corticoids averaged 0.31, and the 17-ks. 1.5 mg/24 hrs. During the treatment the corticoids increased to an average of 2.40 mg/24 hrs., the maximum being 4.23 mg/24 hrs. The corresponding values for the 17-ks. were 3.7 and 5.7 mg/24 hrs.

Case 6. In the two treatment periods a moderate, but only temporary, effect on the joints was seen. There was no effect on the eosinophils or on the sedimentation rate. The sites of injection were infiltrated and sensitive. Only a slight increase of the steroid excretion was observed.

Case 7. The treatment of this patient followed another plan, and he presents various points of interest. His disease was of a very active character, with pronounced swelling and tenderness of many joints, rapidly developing deformities, very high sedimentation rate, and raised temperature.

At first he was treated for one week with ascorbic acid (5 g daily), but this had no beneficial effect; on the contrary, the joints rather became worse. The administration of ascorbic acid was continued (Fig. 4), and during the next 15 days ACTH was administered, 2 I. U. daily. This made the tenderness of the joints disappear, but no significant effect on the mobility or on the deformities was observed, and the sedimentation rate was only slightly influenced. The dosage of ACTH, then, was increased to 24 I.U. daily (divided into 4 daily injections), with dramatic effect: The swelling of the joints disappeared, together with the deformi-

ties, and the mobility was greatly improved. The sedimentation rate decreased to normal values. Towards the end of this period his abdomen become distended without signs of ascites. On X-ray examination a slightly abnormal picture of the small intestine was found, probably due to edema of the intestinal wall. It disappeared after a month. The stools were normal. The last day of treatment a big abscess appeared in the upper eyelid. This was treated successfully with parenteral penicillin. After discontinuance of treatment no relapse was seen, except for a very slight swelling of some of the joints, which appeared a month later. The sedimentation rate rose to 20 mm/1 hr., and continued to be within the range of 20—30 mm during his stay in the department. He was discharged 3 $^1/_2$ months later, still in excellent condition.

The pre-treatment level of corticoids and 17-ks. in the urine averaged 0.40 and 1.8 mg/24 hrs., respectively. Ascorbic acid in itself had no effect on the hormone excretion. During the first part of the ACTH treatment, when the dosage was 2 I. U. daily, a very slight increase of the corticoid excretion was seen, the average being 0.53 mg/24 hrs., whereas the 17-ks. output did not rise (average: 1.0 mg/24 hrs.). It is highly probable that a hypertrophy of the adrenal cortex developed during this part of the treatment, thus making possible the vigorous response to the higher dosage during the next days: When 24 I. U. daily were administered, the corticoid excretion increased enormously, reaching a maximum of 9.90 mg/24 hrs., or 25 times the pre-treatment value, whereas the excretion of 17-ks. increased to a lesser degree, the maximum being 8.8 mg/24 hrs., or 5 times the initial value. It is difficult to ascertain whether or not the ascorbic acid has played any rôle in this reaction. No effect can, in our opinion, be attributed to the cholesterol.

Comment

Thus we have obtained a good effect in 8 of 10 series (case 1, 3: 2nd and 3rd series, 5, 6: both series, 7), but in 5 of those (case 1, 3: 2nd and 3rd series, 6: both series) the symptoms recurred with reduction of dosage or withdrawal of therapy. In one case the effect was more or less durable, except for a moderate relapse occurring after two weeks, and in only one case (no. 7) the remission was maintained for a long period (at least 3$^1/_2$ months) after withdrawal of therapy.

Six patients had deformities. These were corrected in 3 cases, as we had hoped, while in 3 other cases no improvement was seen; in two of these the deformities proved to be due to osseous ankyloses.

The reason why no relapse was seen in case 7, in contrast to the other cases, is probably one of the following. (1) The hypertrophy of the adrenal cortex developing during ACTH therapy was probably greater in case 7, owing to the peculiar scheme of treatment, and it cannot be excluded that the changed state of the adrenal cortices may be maintained to some extent after withdrawal of treatment. (2) It may be due to the pronounced activity of the arthritis in this case, as the best effect would be expected in cases with the greatest resemblance to acute rheumatic fever.

Side effects: In three of the patients (case 4, 5, and 6) the sites of injection were infiltrated and sensitive and one patient (case 7) had a palpebral abscess and displayed signs of edema of the intestinal wall. In two cases, low serum potassium was observed (case 1: 11.1 mg per cent, and case 7: 12.2 mg per cent). After this observation potassium was administered daily during ACTH treatment, as mentioned before, and no cases of low serum potassium were encountered thereafter.

In the case published by ASTRUP *et al.* albuminuria developed during the ACTH treatment, and this proved to be due to amyloidosis. None of the cases in the present series got albuminuria.

In all the cases the excretion of corticoids paralleled the clinical effect more closely than the excretion of 17-ks. Further details on this subject will be published in another paper.

Conclusions

It is the general opinion that in the future the indications for ACTH treatment in rheumatoid arthritis will be considerably more restricted than the first promising results seemed to promise.

According to our experience this also holds true in regard to the juvenile rheumatoid arthritis. One indication, however, does remain: in children in whom deformities are developing, ACTH (or cortisone) is almost imperatively indicated.

In cases where deformities have already developed it is often difficult to decide clinically or roentgenologically, whether or not the deformities are due to osseous ankyloses. In cases where the

presence of osseous ankylosis has not yet been demonstrated, ACTH (or cortisone) should be tried.

It is our experience that, in children, the corticoid excretion is the most reliable measure of response of the adrenal cortex to ACTH.

Acknowledgement

We are greatly indebted to the National Danish Association against Rheumatic Diseases for having supplied part of the ACTH employed.

Summary

Seven patients, aged 2 $^1/_2$—12 years, suffering from juvenile rheumatoid arthritis were treated with ACTH, each patient receiving 1—3 series of injections (total: 10 series). Eight of these series induced remissions, but in only one case the effect was permanent (observation time: 3 $^1/_2$ months). This patient had a very active arthritis, and he received a preliminary treatment with small doses of ACTH, probably causing a hypertrophy of the adrenal cortex, which may account for the good response.

The administration of ascorbic acid, 5 *g* daily, and cholesterol, 1—1 $^1/_2$ g daily, had no demonstrable clinical effect.

Six patients had deformities. In three of these a correction of the deformities was obtained. In two of the remaining three cases they proved to be due to osseous ankylosis.

The authors are of the opinion that ACTH is indicated in cases where deformities are developing, and also when deformities have already developed, if these have not yet been ascertained to be due to osseous ankylosis.

ACTH dans le traitement des arthrites rhumatismales juvéniles.

Sept malades souffrants d'arthrites rhumatismales juvéniles (agés de 2 $^1/_2$ à 12 ans) furent traités par l'ACTH, chaque patient recevant une à trois séries d'injections (au total: 10 séries). Huit parmi ces séries produirent des rémissions, mais dans un cas seulement l'effect fut permanent (temps d'observation: 3 $^1/_2$ mois). Ce malade était porteur d'une arthrite très évolutive et il recut d'abord un traitement préliminaire fait de faibles doses d'ACTH, qui eurent peut-être pour effet une hypertrophie du cortex surrénale qui peut expliquer la bonne réponse au traitement. Un apport quotidien de 5 gr d'acide ascorbique et de I à

1,50 gr de cholestérol n'eut pas d'effet clinique net. Six des malades étudiés avaient des déformations. Parmi trois d'entre eux on obtint une correction de celles ci. Dans deux des trois cas restant, ces déformations étaient dues à des ankyloses osseuses. Les auteurs pensent que l'ACTH reste indiqué dans les cas développant des déformations, et aussi dans ceux pour lesquels elles sont déjà constituées, mais à condition qu'on ne puisse affirmer qu'elles sont sous la dépendance d'une ankylose osseuse.

ACTH in der Behandlung von rheumatoider Arthritis bei Jugendlichen.

Sieben an jugendlicher rheumatoide Arthritis leidende Patienten im Alter von 2 $^1/_2$—12 Jahren wurden mit ACTH behandelt, jeder Patient bekam 1—3 Injektionsserien (im ganzen 10 Serien). Von diesen Serien führten acht eine Besserung herbei, aber nur in einem Fall war die Wirkung dauernd (Beobachtungszeit: 3 $^1/_2$ Monate). Dieser Patient hatte eine sehr aktive Krankheit, wurde zuerst mit kleinen Gaben von ACTH behandelt, wodurch wahrscheinlich eine Hypertrophie der Nebennierenrinde entstand; dies könnte die gute Reaktion erklären. Die tägliche Zufuhr von 5 g Askorbinsäure und 1—1$^1/_2$ g Cholesterol hatte keine klinisch bemerkbare Wirkung. Bei sechs Patienten waren Missbildungen vorhanden. Bei drei von diesen wurde eine Verbesserung der Missbildungen erreicht. Bei zwei der übrigen drei Fälle entstanden die Missbildungen infolge von Knochengelenkssteifigkeit. Die Verfasser sind der Meinung, dass ACTH in solchen Fällen angezeigt ist, bei denen sich Deformiteten entwickeln beginnen, aber auch dann, wenn solche vorhanden sind, falls man nicht sicher ist, dass sie der Knochengelenkssteifigkeit zuzuschreiben seien.

Tratamiento de la artritis reumatoidea juvenil con ACTH.

Siete niños de edad comprendida entre 2 $^1/_2$—12 años afectos de artritis reumatoidea juvenil fueron tratados con ACTH, recibiendo cada paciente 1—3 series de inyecciones (total 10 series). Ocho de estas series produjeron remisiones, pero tan solo en un caso el efecto fué duradero (tiempo de observación: 3 $^1/_2$ meses). Este enfermo afecto de una artritis muy activa y que había ya recibido un tratamiento con pequeñas dosis de ACTH probablemente tenía una hipertrofia de la corteza suprarrenal por lo cual la respuesta fué muy favorable. La administración suplementaria de ácido ascórbico y colesterol a las dosis de 5 g y 1—1 $^1/_2$ g diarios respectivamente no mostró tener ningún efecto clínico. Seis enfermos presentaban deformidades y en 3 de ellos pudo obtenerse una buena corrección; en 2 de los 3 casos restantes estas deformidades eran debidas a anquilosis óseas.

Los autores son de la opinión que el ACTH está indicado en los casos en los cuales las deformidades están en curso de producirse o también cuando ya se han desarrollado y se tiene la impresión de que no se ha producido uns anquilosis ósea.

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CASE REPORT

Report of Two Cases of Acrodynia Appearing After Calomel Theraphy but Without Excretion of Mercury in the Urine and Cured With B. A. L.

by

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The etiology of acrodynia was an open question until the recent discoveries of WARKANY (7) and FANCONI (4) which seemed at last to give an answer to this question. By various ways, they came to the conclusion that acrodynia was the result of a sensitization to some mercury compounds, chiefly calomel (mercury chloride) frequently found in the teething powders and vermifuges in common use. One of the reasons for this assumption was the frequency with which these authors found a history of the use (and abuse) either of mercuric teething powders or of vermifuges. Another was the finding of abnormally high quantities of mercury in the urine of patients suffering from acrodynia. Therefore, BIVINGS and LEE (2) tried and succeeded in curing cases of acrodynia with B. A. L. Recently, BIVINGS (1) concluded, after a survey of the literature on the subject that on the whole, B. A. L.-therapy gave excellent results in the treatment of pink disease: of 15 cases treated with B. A. L. 11 improved rapidly, the remaining 4 more slowly. In a recent paper, FANCONI and BOTSZTEJN (4) used the fact that pink disease reacts so favorably to B. A. L. therapy as an argument for their theory. Nevertheless, it seems that a positive response of a case of acrodynia to B. A. L. therapy is not necessarily a convincing argument that the etiology is always a sensitization to mercury.

We had recently the opportunity of studying two cases of acrodynia under B. A. L. treatment, and during recovery we were able to observe a curious phenomenon.

Case Histories

1. Jeanine G.... Girl, 2 $^1/_2$ years old, was referred by her doctor because she had became more and more fretful during the previous two or three weeks; she cried night and day, asking her parents to rub the palms of her hands and the soles of her feet or to put them in cold

water. The parents added that the hands and feet were red and cold for about three weeks and that apparently the baby was in great discomfort. She had no appetite, did not play and always wanted to go to bed. Physical examination showed red, tense, cold palms and soles, and there was some peeling at the tip of some of the fingers. The child was not cooperative but did not cry; nevertheless the pulse rate was 170 per minute. It was impossible to take the blood pressure, but there was no doubt that the child was suffering from acrodynia, showing the pathognomonic triad: tachycardia, change in the temperament, dermatological lesions. Another fact supported the diagnosis: the parents acknowledged having given the child, three weeks ago, a vermifuge consisting mainly of santonin and calomel, the dose being 150 milligrams of each.

2. Pierre Sim. . . . Boy, 2 1/2 years old, was brought in by his parents complaining of a change in his temperament and swollen hands. Both palms and soles were red, tense and moist, and the back of both hands were oedematous. The pulse rate was over 190. When questioned about previous treatment, the parents admitted that the child had not been given any drugs during the last six months, "except for calomel powders, prescribed by the family doctor for the child's constipation".

For psychological reasons, admission to hospital was refused by the parents in both cases. A large dose of pyridoxin was given as "home" treatment as FRONTALI (5) claimed excellent results with this therapy. Both mothers came back a week later: the children's condition was worse than ever, and the patients were admitted to the pediatric department. Both children received B. A. L. using BIVING's dosage, i.e., 25 mg per kg of body weight every four hours for two days, every six hours for the next two days, and thereafter, every twelve hours for eight days.

Both cases showed dramatic improvement and a fortnight later, they were discharged, in exellent condition.

The history of these two patients shows nothing essentially new and is merely a confirmation of BIVING's work. The laboratory findings are more confusing.

We have used for our determinations a polarographic method elaborated by PONSART (6). For more details of this technique, we refer to the work to be published by PONSART.

Using this method (which gave excellent results in other circumstances) we were unable to find any trace of mercury in the urine of either child, either before or during treatment with B. A. L. The urine was collected, as completely as possible, for 24 hours and immediately tested for mercury, twice before starting the B. A. L. therapy and thereafter, every day during treatment. It seems noteworthy to mention that beginning from the second day of the treatment, the daily output of urine was more than doubled.

Discussing the report of WARKANY and HUBBARD (8), BOYD (3) described briefly a case of acrodynia (sent to him by the family doctor) in which the urineanalysis failed to show the presence of mercury. Nevertheless, the family doctor tried B. A. L. injections which cured the child.

In addition to this case with a negative finding for mercury *before* treatment, our two cases showed the same absence of mercury not only before but even *during* the B. A. L. therapy. The B. A. L. had a very beneficial action in these cases, although there was no demonstrable mercury excretion in the urine. This fact suggests that B. A. L. may act in a way different than hitherto believed (WARKANY and FANCONI).

Summary

Report of two cases of acrodynia appearing three and five weeks after ingestion of calomel are reported. Treatment with large amounts of pyridoxin was ineffective, but the two children recovered quickly after B. A. L. therapy. Using a specific and sensitive method (polarography) no mercury could be found in the urine passed before and during B. A. L. treatment. The author questions if the WARKANY-FANCONI theory of acrodynia being a sensitization to some mercury salts is not too dogmatic to fit to all cases of acrodynia.

Deux cas d'acrodynie, apparus après ingestion de calomel mais sans mercure dans les urines, curés par le B. A. L.

Description de deux cas d'acrodynie, survenus dans un délai de trois à cinq semaines après ingestion de calomel d'une part, d'un vermifuge à base de santonine et de calomel d'autre part. Un essai de traitement par de fortes doses de vitamine B 6 suivant FRONTALI n'a donné aucun résultat, mais on observe une guérison rapide après traitement par le B.A.L. Chose curieuse, dans aucun des deux cas une méthode polarigraphique à la fois très sensible et très spécifique de dosage, n'a permis de metter en évidence la moindre trace de mercure dans les urines, ni avant ni pendant le traitement par le B.A.L. On est donc en droit de se demander jusqu'à quel point les rapports entre l'acrodynie, la sensibilisation au mercure et leur traitement par le B.A.L. sont sussi simples que le laissent supposer les théories défendues par WARKANY et FANCONI.

Zwei Fälle von Akrodynie, aufgetreten nach Behandlung mit Kalomel aber ohne Quecksilberausscheidung im Harn, geheilt durch B. A. L.

Beschreibung von zwei Akrodynie-Fällen, die einige Wochen nach Kalomelbehandlung bzw. Wurmpulvern (Santonin und Kalomel) beobachtet wurden. Kein Erfolg mit hohen Gaben Pyridoxin (Therapie nach FRONTALI), rasche Besserung aber nach B.A.L.Therapie. Mit Hilfe

von einer polarographischen Methode (empfindlich und spezifisch!), war es jedoch unmöglich die kleinste Quecksilberausscheidung im Harn, weder vor noch während die B.A.L.Therapie nachzuweisen. Der Verfasser fragt sich ob die Theorie, dass die Akrodynie eine Quecksilbersensibilisierung ist (FANCONI und WARKANY), nicht zu dogmatisch ist.

Communicación de 2 casos de acrodinia aperecidos tras terapéutica con calo melanos, sin excreción de mercurio en la orina y curados con B. A. L.

Se comunican 2 casos de acrodinia aparecidos 3 y 5 semanas respectivamente de haberse practicado un tratamiento con calomelanos. El empleo de grandes cantidades de piridoxina, de acuerdo con el método de Frontali se mostró inefectivo, curando ambos completamente después de un tratamiento con B.A.L. Empleando un método polarográfico específico y muy sensible no pudo hallarse mercurio en la orina ni antes, durante o después del tratamiento con B. A. L. El autor se pregunta si la teoria de Warkany-Fanconi de condiderar la acrodinia como resultado de una sensibilización frente a algunas sales mercuriales no es demasiado esquemática para aplicarse a todos los casos de esta enfermedad.

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Lipochondrodystrophy (Gargoylism, Hurler's Syndrome) with Specific Cutaneous Deposits

by

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Gargoylism or Hurler's syndrome is a condition characterized by chondrodystrophic changes and the formation of lipoid deposits in various tissues and organs. The term *lipochondrodystrophy* has therefore been adopted in Anglo-American countries.

A considerable number of publications on gargoylism exist. STRAUSS (3) in 1948 collected 119 cases from the literature and reported a further one. Autopsy reports exist in a large number of cases, and the presence of peculiar vacuolized cells in the interior organs has been pointed out as a characteristic feature. These cells are mainly found in the liver and lymph nodes, but they may occur in the spleen, cardiac muscle, lungs, cornea, and endocrine organs as well.

The chemical nature of the deposits is not known. KRESSLER and AEGERTER (1) made careful studies with regard to this point in their case. Mucicarmine stain, Best's glycogen stain, fat stains and lipoid stains all gave negative results.

Nor could birefringence be demonstrated. The substance, however, is assumed to be lipoid in nature, and KRESSLER and AEGERTER consider the disease "a metabolic dysfunction of one of the complex lipoides".

We have not been able to find any statement as to the occurrence of lipoid deposits in the skin in lipochondrodystrophy, for which reason the following case may be of interest; it has been reported previously by NJÅ (2) among 5 cases of sex-linked gargoylism.

The patient was a $6\ ^1/_2$ year old boy in whom mental deficiency was noted at the age of 2. His height was below the normal for his age. The head was large, the facial features coarse, and the neck short, and there was considerable kyphosis. Limitation of movements and deformity of the large joints, particularly the shoulder joints, were present, and the finger joints were the site of flexion contractures. The liver and spleen were enlarged. Corneal opacities were not present.

The patient had a peculiar *skin lesion* (Figs. 1 and 2) consisting of numerous nodules symmetrically distributed in an area of about 6 by 10 cm extending from the angle of the scapula towards the axillary line. The nodules were of the size of a pea and of a firm consistency. At the

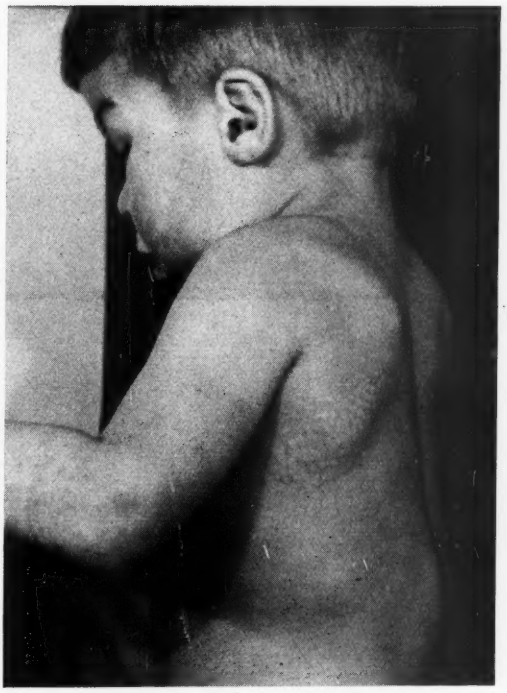

Fig. 1. Gargoylism with skin lesion.

site of the nodules, the skin was paler than normal, probably depigmented, with an appearance resembling that from pressure of a coarse cloth.

A biopsy specimen was taken from the affected area. Usual paraffin sections were cut out and stained with hematoxylin-eosin. Outstanding microscopic features were thickening of the dermis and abundant hyaline or collagenous fibres arranged in bundles, which in the deep layers of the skin were widely separated and showed an irregular fragmented appearance. The bundles stained intensely red with eosin, some of them with a shade of violet. The epithelial membrane showed evidence of nutritive disturbances and slight hyperkeratosis, but was of normal thickness. Beneath the epithelium in close relation to its basal layer were seen some cells with a vacuolized cytoplasm and irregular partly pyknotic nuclei. These cells appeared almost as punched-out areas in the tissue.

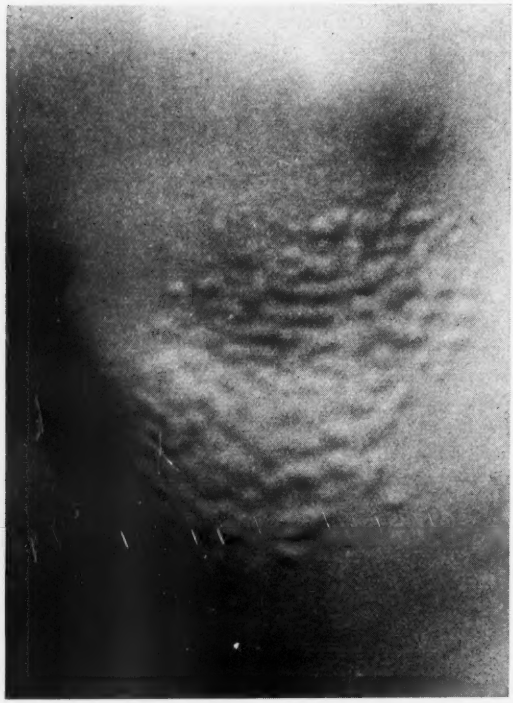

Fig. 2. Gargoylism with skin lesion.

In an effort to determine the nature of the substance filling the vacuoles described, sections were stained for lipoids according to the Lorrain Smith-Dietrich method, while frozen sections were stained with Sudan III. Both methods, however, gave negative results. Nor could birefringence be demonstrated.

On the basis of descriptions and illustrations of vacuolized cells, the cells observed in the present case seem quite identical with those appearing in the internal organs (liver, spleen, lymph nodes, cardiac muscle, lungs, cornea and endocrine organs) in gargoylism.

STRAUSS has pointed out the presence of connective tissue changes with proliferation of collagenous fibres, in the internal organs, cardiovascular system, and skeleton. Swelling of the intima and media of the large and medium-sized arteries is said to be a characteristic feature.

Fig. 3. Photomicrograph of skin, small power view. Note considerable thickening of derma and abundant formation of collagenous bundles.

Fig. 4. Photomicrograph of skin, large power view, showing vacuolized cells beneeth the epithelium.

The thickening of the dermis observed in the present case might be interpreted as a similar phenomenon.

Summary

A peculiar skin lesion in a 6 1/2 year old boy with gargoylism is described. Biopsy showed vacuolized cells just below the epithelial membrane. These cells had the same microscopic appearance as those appearing in the internal organs of patients with gargoylism who have died. They also reacted in the same manner to various stains. A considerably increased thickness of the dermis with abundant formation of hyaline and collagenous bundles was also observed.

Lipochondrodystrophie (Gargoylisme ou syndrome de Hurler) avec dépots spécifiques cutanés.

Une lésion cutanée particulière est décrite chez un garcon agé de 6 ans 1/2 porteur d'une maladie de Hurler. La biopsie montra des cellules vacuolaires situées juste au dessous de la couche épithéliale. Ces cellules avaient le méme aspect que celles que l'on peut retrouver dans les organes de malades morts de cette affection. Elles présentaient les mêmes affinités tinctoriales que ces dernieres. On pouvait observer de plus un épaississement considérable du derme de mème qu'une formation abondante de fibres collagènes et hyalines.

Lipochondrodystrophie (Gargoylismus, Hurler'sche Krankheit) mit eigenartigen Hautablagerungen.

Es wird eine eigenartige Hautstörung bei einem 6 1/2 jährigen Knaben mit Gargoylismus beschrieben. Eine Probeexcision wies vakuolenartige Zellen knapp unterhalb der Deckzellenschichte auf. Diese Zellen glichen mikroskopisch vollkommen jenen, welche in inneren Organen von an Gargoylismus verstorbenen Patienten auftauchen. Sie reagierten in gleicher Weise auf verschiedene Färbungsmethoden. Es wurde auch eine starke Zunahme an Dichte der Lederhaut mit reichlicher Bildung von hyalinen und kollagenen Bündeln beobachtet.

Lipocondrodistrofia (gorgolismo, síndrome de Hurler) con depósitos cutáneos específicos.

Se describe en un niño de 6 1/2 años afecto de gorgolismo unas lesiones cutáneas peculiares. La biopsia mostraba células vacuolizadas justo debajo de la membrana epitelial, teniendo dichas células el mismo aspecto microscópico que las células que se encuentran en los órganos internos de pacientes fallecidos de gorgolismo. Estas células respondían también de un modo análogo ante diversas coloraciones. Se observaba también

un considerable aumento de espesor del dermis con abundante formación de bandas de substancia hialina y colágena.

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Misleading Results of Pneumoencephalography in an Infant with Severe Hypoglycemic Attacks

by

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The value of pneumoencephalography as an indicator of abnormalities in the brain is seriously limited by the difficulty in obtaining reliable information about findings in normal subjects and normal variations. This refers primarily to conclusions drawn from the roentgenograms concerning the trophic condition of the cerebral cortex. Anybody familiar with this diagnostic method knows that filling of the subarachnoid space with air is a capricious procedure, and that a picture showing no air over the surface of the brain does not allow the conclusion that atrophy is absent. It is less well known, perhaps, that even large accumulations of air over the surface may be mere artefacts when observed in children less than 6 years old. The following case is therefore presented as an illustration.

Case report

J. no. 80/51. A three months old boy, born March 15, 1950, was admitted to the University Clinic of Pediatrics, Copenhagen, because of attacks during which he would cry, turn pale and could not be aroused.

His eyes turned upwards or converged, and slight convulsive movements of his limbs were seen. After 10 to 30 minutes he would appear normal again, except for sweating and languor.

The family history was negative, without any case of epileptic disorder. The pregnancy was uneventful. Delivery was normal, and the birth weight was 4150 g. There were no signs of asphyxia. The baby sucked well and gained in weight satisfactorily. He was healthy except for a suppurative otitis in June 1950 which was treated with penicillin.

His symptoms were found to be caused by severe falls in blood sugar, sometimes to values below 20 mg per cent, following the initial postprandial rise. Several fasting values were found below 30 mg per cent. Subcutaneous injection of 0.1 mg adrenalin caused either no rise in blood sugar, or, at a later examination, only a slight rise (from 37 up to 73 mg per cent). However, a rise from 34 to 123 mg per cent was seen when glucose was given simultaneously by duodenal tube. After two hours this was followed by a fall to 26 mg per cent followed by an attack. The adrenalin injection caused a fall in the number of circulating eosinophils from 44 to 25 per cubic millimeter — at a later examination from 112 to 19. Twenty milligrams of ACTH caused no definite rise in blood sugar; the number of eosinophils dropped from 100 to zero. The following diagnostic procedures and tests gave only normal findings: hemoglobin determination, sedimentation rate, urine analysis for sugar and albumin, Wassermann reaction, eye-ground examination, X-ray studies of skull, oesophagus, stomach, and duodenum. A roentgenogram of the abdomen after insufflation of air into the stomach offered no suggestion of tumour in the pancreas, nor could any such tumour be found on palpation. The liver was not enlarged. The thymol turbidity test was normal. The glycogen content of the blood was 5 mg per cent. Two electroencephalograms showed nothing which could be clearly classified as abnormal for the age. An electrocardiogram was normal, though with a negative T wave in the third lead.

The only way of guarding the baby against attacks was to supply a continuous administration of food rich in glucose through a duodenal tube.

The patient was temporarily transferred to the neurosurgical department at the age of five months. A pneumoencephalogram was made through a suboccipital puncture, 25—30 ml liquor being replaced by 20 ml filtered air. The pictures (Fig. 1—2) showed a wide mantle of air separating the left hemisphere from the cranial wall, the gyri and sulci being visible with marked outlines.

A tentative diagnosis of severe atrophy of the left hemisphere, caused by occlusion of the left middle cerebral artery, was proposed. It was supposed that the arterial supply of the hypothalamus through branches of the anterior communicating artery was similarly compromised,

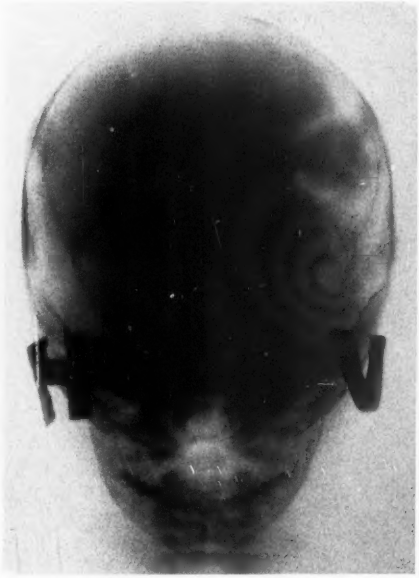

Fig. 1. Suboccipital encephalogram, antero-posterior view, showing large mantle of air over left hemisphere.

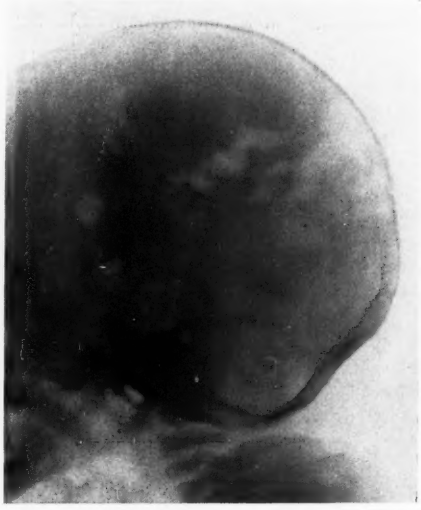

Fig. 2. Same, lateral view, showing large accumulations of air over the cortex.

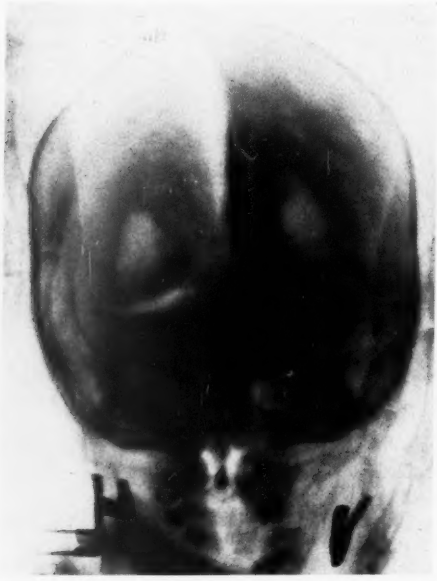

Fig. 3. Ventriculogram showing subarachnoid (and subdural?) air over right hemisphere.

Fig. 4. Same, prone, showing large mantle of air over the posterior part of the brain.

giving rise to disturbances in the blood sugar regulation. Some scepticism was, however, maintained as to the validity of the diagnostic conclusions. The lack of any manifest right-sided motor disturbances at the time of examination was surprising, if a severe atrophy of the left hemisphere, including the motor area, were really present. Secondly, although *rise* in blood sugar from hypothalamic origin is a well-known fact, and although *moderate hypoglycemia* undoubtedly may be due to disorders of the hypophysis (Simmonds' disease) and the hypothalamic region, probably through destruction of anti-insulin producing cells, we still had to admit that we could not find reports of such *severe* disturbances in the blood sugar regulation as found in this baby, resulting from brain pathology.

In view of these considerations and because our reservations could be further supported by the observations of ZELLWEGER, mentioned below, we considered an explorative laparotomy necessary. This was done by Dr. C. C. Winkel Smith. No tumours of the pancreas were found by palpation of the organ. Two thirds of the gland were excised, as a partial amputation of the insulin-producing organ was considered the only chance for the child to regain a normal regulation of the blood sugar level. No adenomas were found by microscopical examination. The operation resulted in definite clinical improvement, lasting one week, with a blood sugar level between 200 and 300 mg per cent. After this short period, however, a complete relapse followed with recurring hypoglycemic attacks and convulsions.

As MCQUARRIE & *al.* and THORN & *al.* have reported beneficial effect of ACTH on idiopathic hypoglycemia, ACTH was tried in the present case for a period of 7 days, with a dosage of 24 mg daily in the first 3 days and then 14 mg daily, divided into four intramuscular injections with 6-hour intervals. During the first days of this treatment the blood sugar level was slightly higher and the attacks less frequent, but this slight effect ceased as soon as the dosage was lowered.

On December 20, a slight right-sided hemiplegia was disclosed by neurological re-examination, and the possibility of a cerebral cause for the hypoglycemia was again discussed, in spite of our earlier doubts. As no filling of the third ventricle was visible on the first pneumoencephalogram, the baby again was transferred to the neurosurgical department at the age of 8 months. On January 20, 1951, ventriculography was performed by puncture of both posterior horns. 85 ml of liquor was replaced by air. The result was surprising (Fig. 3—4). In addition to a diffuse dilatation of both lateral ventricles, large areas of air were found over the *right* hemisphere, probably partially located in the subdural space. The third ventricle was filled, and the interpeduncular space looked normal. Over the left hemisphere, however, no air was found. It was considered impossible that any confusion between right and left might

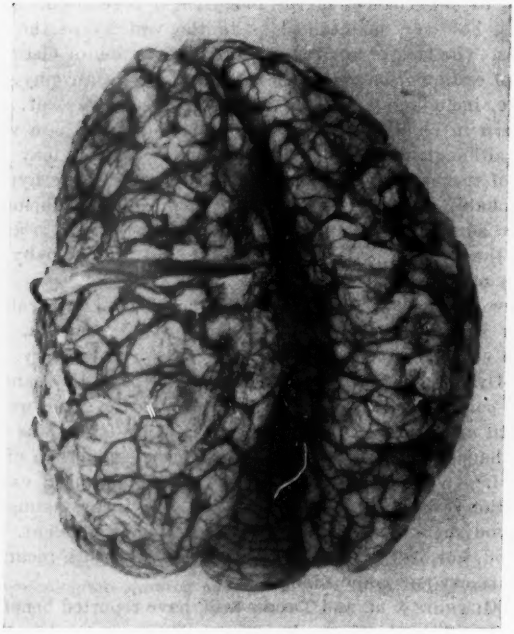

Fig. 5. Brain, without significant cortical atrophy.

have occurred during either this or the earlier procedure. If our confidence in this diagnostic procedure were justified, we had to conclude from those two air-studies that a severe bilateral cortical atrophy was present, and that its shifting localization from left to right on the roentgenograms was due to "accidental" factors.

The baby was discharged on a diet rich in carbohydrates, and on moderate doses of phenobarbital. He died at the age of 10 months in the County Hospital, Copenhagen, where he had been admitted for an otitis.

At autopsy, bronchopneumonia and a pleural empyema were found on the left side. Microscopical examination of the remaining part of the pancreas revealed no adenomas. The thyroid gland and the hypophysis showed no microscopical abnormalities. The adrenal medulla was somewhat hyperplastic, but the adrenal cortex was normal. Sections from liver and kidney showed only venous congestion. (These examinations were performed by Dr. A. Soeborg Ohlsen).

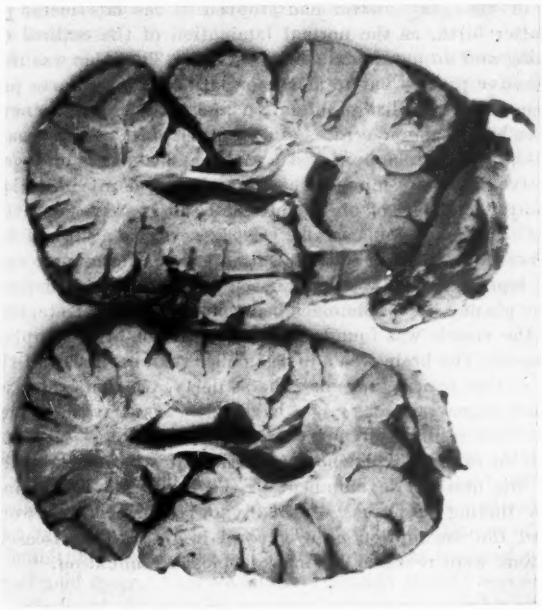

Fig. 6. Two transverse sections of the brain. Partial compression of the hemispheres has occurred during preparation. No significant atrophy of the cortical zone is visible.

The brain weighed 650 g (after fixation in 10 per cent saline-formaldehyde solution). Except for some very small areas of shrinkage in a few convolutions between the middle and the inferior frontal gyrus and in the right central sulcus, no atrophy was found which in any way corresponded to the massive atrophy suggested by the air-studies (Fig. 5–6). On sections a moderate dilatation of the anterior horns was seen. The third ventricle, too, was dilated, and a small recess was found at the hypophyseal fossa, bulging over the optic chiasma. The aqueduct of Sylvius was dilated.

Several microscopical sections were prepared from the right basal ganglia, beginning anterior to the third ventricle and continuing backwards to the cerebral peduncle. Sections were also prepared from the temporal cortex on both sides, from the motor area on the right and left side, and from the medulla oblongata.

Microscopical examination of the brain revealed diffuse hyperemia and edema, but no signs of inflammation. It also showed that the devel-

opment of the gray matter had stopped in the late foetal period or shortly after birth, as the normal lamination of the cortical cell layer was lacking and no pyramidal cells were seen. That this was not due to a degenerative process but to an abnormal development was proved by the absence of both glial proliferation and atrophy of the nerve cells.

In the hypothalamic centres and in other parts of the basal ganglia the developmental stage appeared normal, and no signs of degeneration of the nerve cells were found. There was incipient myelinisation of the white matter, and foci of oligodendroglial cells were seen in the neighbourhood of the ventricular walls; this, however, is a normal finding in infants' brains, in which the myelinisation has not yet been accomplished.

The leptomeninges were undifferentiated, no sharp distinction between the pia and the arachnoidea being demonstrable. Here, too, hyperemia of the vessels was found, but no infiltration with lymphocytes.

Comment: The brain was a little smaller than normal, and the development of the cortical gray matter was delayed, but no signs were seen of any such degeneration as might have been caused by the hypoglycemic attacks or the resulting hypoxia or anoxia of the brain (see COURVILLE). We have no further experience suggesting any pathogenetical relation between the delayed development of the brain and the hypoglycemic state. A finding of lesions of the hypothalamic centres would have supported the assumption of a cerebral origin of the disease, but no such lesions were revealed by microscopical examination.

Discussion

In our opinion, the only reasonable conclusion from our observations is that the large subarachnoid accumulations of air found over the left, and later over the right hemisphere are artefacts. These may be due partly to the great softness of the infantile brain, owing to its high content of water, and partly to the comparatively large part of the skull cavity being occupied with liquid in the infant. The force of gravity would result in the air being situated in the topmost part of the skull.

Examples of the unreliability of pneumoencephalography in infancy have been reported by other authors. ZELLWEGER studied 5 infants aged 3, 4, 6, 14 and 21 months, respectively. Wide-spread accumulations of air were demonstrable in the subarachnoid space, and this was found to be in accordance with the clinical diagnoses: idiocy, cerebral sclerosis, cerebral palsy and epilepsy. Repeated air-studies, however, at the ages of 1, 2 3/4, 1 3/4, 6 and 3 3/4 years, respectively, failed to show any subarachnoid air at all. The author concluded that the first findings had been artefacts. ZELLWEGER cites similar observations as seen in our case (WEBER, 1929, ELLI SAMER, 1934). The last cited author had insufflated air on infants after death; she found that the air had accumulated

over the highest part of the brain and moved to other places when the posture was altered.

According to ZELLWEGER, misleading air accumulations in the subarachnoid space are rare after the second year of life, although they may be met with in children up to 6 years.

This is not the same as mistakes due to *subdural* insufflation of air during the pneumoencephalography. These are found at any age, and they are not very rare.

Acknowledgment. We are much indebted to Dr. BENT BROAGER, head-assistant of the Neurosurgical Department of The University Hospital, Copenhagen, for permission to publish roentgenograms as well as case-record notes from the patient, and to Dr. A. SOEBORG OHLSEN, The County Hospital, Copenhagen, for the autopsy report.

Summary

In a five months old infant with a severe non-pancreatogenic hypoglycemia of unknown pathogenesis, an encephalogram through suboccipital puncture showed wide areas of air over the *left* hemisphere. A ventriculography performed 3 months later showed a moderate dilatation of the ventricular system as well as large accumulations of air over the *right* hemisphere. On both occasions the air was localized mostly in the subarachnoid space. A severe bilateral cortical atrophy was diagnosed from these findings. At autopsy, however, almost no atrophy was found, a result quite incompatible with the roentgenograms. This observation is in accordance with those of ZELLWEGER and other authors. The authors conclude that subarachnoid accumulations of air, visible on the encephalogram or ventriculogram, are unreliable as a diagnostic guide in infants.

Résultats inexacts donnés par l'encéphalographie gazeuse chez un enfant présentant des accès sévères d'hypoglycémie.

Chez un enfant de 5 mois atteint d'hypoglycémie d'étiologie inconnue mais non pancréatique, une encéphalographie sub-occipitale, montra des espaces vides, occupés par l'air au dessus de l'hémisphère *gauche*. Une ventriculographie pratiquée trois mois plus tard mit en évidence une dilatation modérée ventriculaire de même qu'une accumulation d'air au dessus de l'hémisphère *droit*. Dans les deux cas l'air s'était accumulé surtout dans les espaces sous-arachnoïdiens. On conclut donc à l'existence d'une grave atrophie corticale bilatérale. Mais à l'autopsie on ne trouva aucune trace d'atrophie, résultat qui était totalement incompatible avec les aspects radiologiques enregistrés. Cette observation entre en accord avec celles de Zellweger et d'autres auteurs. Les auteurs concluent que l'accumulation d'air au niveau des

régions sous-arachnoïdiennes, que l'on peut voir sur les clichés radiologiques encéphalographiques ou ventriculaires ne peut être tenue pour guide d'un diagnostique chez les enfants.

Irreleitende Ergebnisse der Pneumoencephalographie bei einem Säugling mit schweren hypoglykämischen Anfällen.

Bei einem fünf Monate alten Säugling mit schwerer, nicht von der Bauchspeicheldrüse ausgehender Hypoglykämie, deren Entstehung und Entwicklung unbekannt war, wies eine Encephalographie nach suboccipitaler Punktion grosse Lufträume über der *linken* Hälfte des Grosshirns. Eine 3 Monate später durchgeführte Ventrikulographie wies sowohl eine mässige Erweiterung des ventrikulären Systems als auch grosse Luftansammlungen über der *rechten* Hälfte des Grosshirns auf. Die Luft war in beiden Fällen hauptsächlich auf den subarachnoidalen Raum beschränkt. Auf Grund dieser Befunde wurde eine schwere beiderseitige Rindenatrophie diagnostiziert. Bei der Sektion wurde jedoch fast keine Atrophie gefunden, ein Ergebnis, welches mit den Röntgenbildern völlig unvereinbar war. Diese Beobachtung stimmt mit den Feststellungen von Zellweger und anderer Verfasser überein. Die Verfasser schliessen daraus, dass die im Encephalogramm oder Ventrikulogramm sichtbaren subarachnoidalen Luftansammlungen als diagnostischer Hinweis bei Säuglingen unverlässlich sind.

Resultados discordantes de la neumoencefalografía en un niño con accesos hipoglicémicos severos.

En un niño de 5 meses afecto de una hipoglicemia severa no pancreática de patogenia desconocida la práctica de una encefalografía por punción suboccipital mostró zones aereas sobre el hemisferio *izquierdo*. Otra ventriculografía practicada 3 meses más tarde mostraba una moderada dilatación de los ventrículos y una amplia acumulación de aire sobre el hemisferio *derecho*. En ambas ocasiones el aire estaba localizado en su mayor parte en el espacio subaracnoideo. En vista de estos hechos se diagnosticó una atrofia cortical bilateral. En la autopsia sin embargo no pudo comprobarse dicha atrofia, hecho por completo incompatible con el hallazgo radiológico. Estas observaciones están de acuerdo con las hechas por Zellweger y otros autores. Llegan a la conclusión que los acúmulos de aire en los espacios subaracnoideos visibles por encefalografía o ventriculografía son métodos inexactos para ser usados como diagnóstico en los lactantes.

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Signs of Sexual Precocity in a Male Infant due to Estrogenic Ointment

by

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An enlargement of the mammae, sometimes of rather considerable magnitude, is commonly observed in the newborn child and in the neonatal period. It is also well known that boys during puberty sometimes show a definite increase in the size of the mammae. On the other hand, in the age interval between the neonatal period and puberty, gynaecomastia seems to be a very rare occurrence. According to a statement by WILKINS in his recent monograph, only one case belonging to this age group had been reported. The finding in that case was caused by an adenoma of the supra-renal glands. In the following a short report is given of a case of gynaecomastia of quite different origin.

Case report

The patient, a boy aged 10 months, was admitted to Akademiska Sjukhuset at Uppsala on Oct. 12, 1950, because of a considerable growth of the breasts in the preceding 5 months. This was associated with an increasing pigmentation of areolae mammae, penis and scrotum. The parents were healthy, except that the mother suffers from an eczema of her hands.

The boy was born at full term, weighing 2 770 grams, and was entirely breast-fed until 6 months' age. His development had been normal. Admission examination revealed him to be 72 cm in length with a weight of 8.8 kg. There was a considerable increase in size of the mammae, both presenting tumors of about 2 cm diameter and 5 mm thickness, presumably glandular tissue (Figure 1). The skin of the areolae mammae, penis, scrotum and around the anus was considerably pigmented. The linea abdominalis was intensely pigmented up to about two cm above the umbilicus (Figures 1 and 2). No other pigmentations were present. A rather thick growth of hair, up to 5 mm in length, was found over a triangular area with its apex at the base of the penis and with a sharp upper border about 25 mm from penis (Figure 3). No other abnormal hair was present. The genital organs were normal in shape and size, and exploration per rectum revealed nothing of pathological significance. The blood pressure was 90/65 mm Hg.

The laboratory tests showed: hemoglobin 12.0 g per cent; R. B. C. 4.0 mil.; W. B. C. 9 800 with a normal differential count; M. S. R. was 5 mm per hour; the urine was entirely normal; the total base content of the serum was 162 meqv/l; potassium 5.1 meqv/l; chlorides 104 meqv/l and cholesterin 147 mg per 100 ml. The Hanger test was faintly positive, Takata negative and thymol test 0.4 units. The glucose tolerance test was normal. An injection of 5 mg ACTH caused a fall in the eosinophilic cell-count from 268 to 34 per cubic mm, while the uric acid-creatinine quotient, (as in normal cases), rose from 6/5 to 67/35.

The urine contained 0.9 mg neutral 17-ketosteroids per 24 hours, but no estrogenic substances were found. X-ray examination of the skull revealed nothing abnormal. The bone-age was normal.

Evidently, the case could be characterized as one of sexual precocity of heterosexual, feminizing pattern, possibly belonging to the adrenogenital syndrome group.

The examinations reported however failed to support the original suspicion, that the physical changes were caused by a hyper-functioning (tumor?) system of internal secretion. Another origin of the reaction seemed more probable. When scrutinizing the anamnesis for the possibility of any hormone preparations having been given to the child, it was revealed that stilbestrol ointment was used in the child's home. The mother had started to use this preparation for her eczema a few weeks before the child's disturbances became noticeable. As the ointment was agreeable to use, she employed it generously each time she washed her hands before nursing the child, so that her hands were quite greasy. In all, during the 5—6 months before the child was admitted, she had used 300 grams of the preparation, which contained 0.1 per cent diethyldioxistilbene.

As it seemed quite possible that the child's condition had resulted

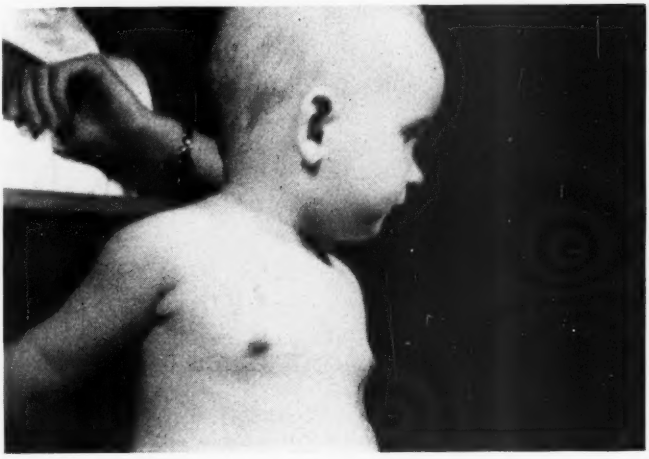

Fig. 1.

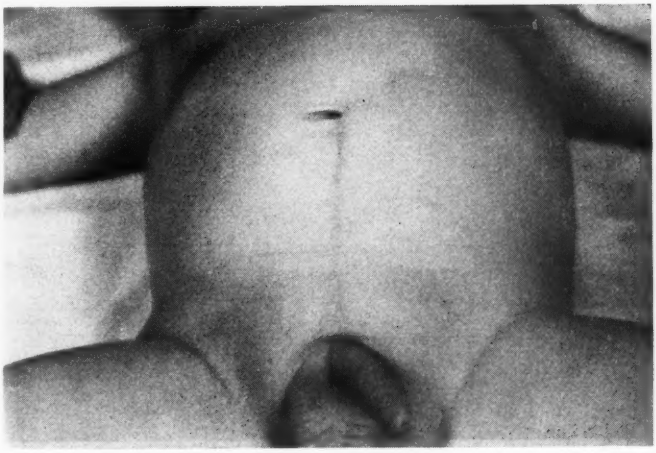

Fig. 2.

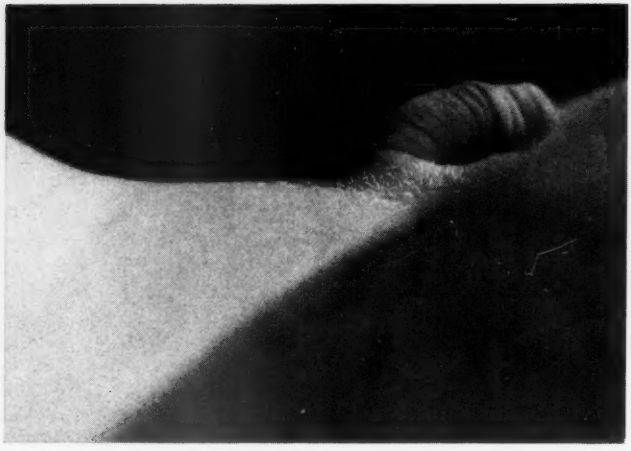

Fig. 3.

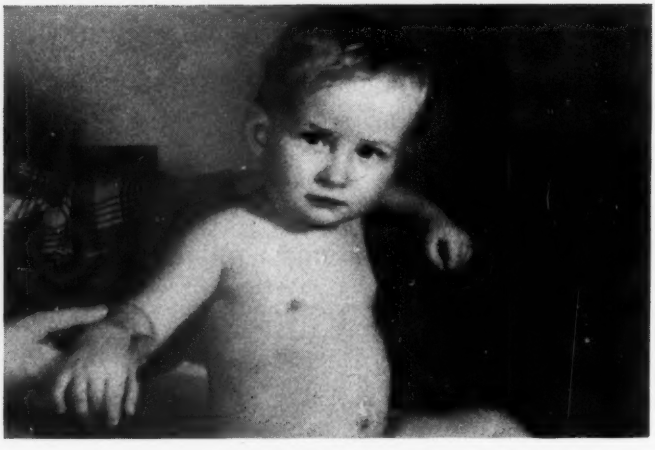

Fig. 4.

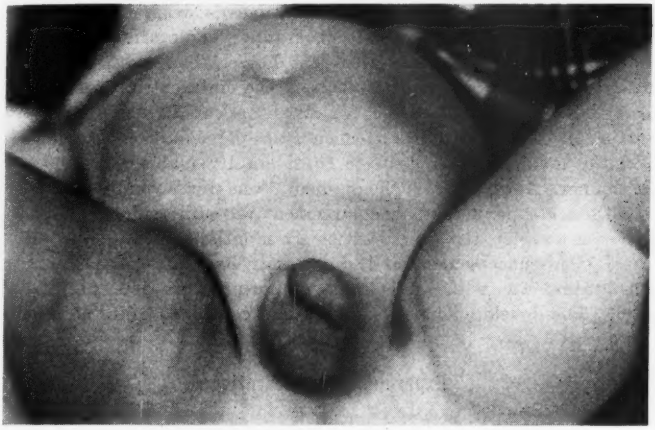

Fig. 5.

Fig. 6.

On admission: Gynaecomastia (Fig. 1), pigmentations (Figs. 1 & 2) and sexual hair (Fig. 3).
Six months later: Normal conditions (Figs. 4, 5 & 6).

from percutaneous absorption of this estrogenic drug, further planned examinations (pneumo-retro-peritoneography, explorative laparotomy) were omitted, and the child was sent home. The mother thereafter nursed her child as before, without using the ointment in question. The observed changes in the child gradually disappeared. Three weeks after cessation of exposure to the ointment, the pigmentation was generally paler, the mammary glands were considerably smaller, and the pubic hair thinner. After 9 weeks, the pigmentations were even less noticeable, and although some mammary enlargement was still evident on one side, there was none on the other. After six months the child was entirely normal, the gynecomastia and pubic hair had disappeared, and the pigmentation was within the limits of normal variation (Figures 4, 5 and 6). The development of the child had continued quite unimpaired.

Experimental observations

Further study of the origin of the syndrome observed was attempted in the following way. A 5 months old boy with a large myelomeningocele, but otherwise well developed and in good condition, was exposed to the same ointment as mentioned above. There was at this time no mammary enlargement, no abnormal pigmentations and no pubic hair. The preparation was rubbed into the skin of the chest, initially in a quantity of about 0.3 grams daily. As no effect was visible after one month, the daily dose of ointment was increased to about 0.7 grams. Two weeks later, an increased pigmentation of areolae mammae with associated gynecomastia was evident on both sides. These findings gradually increased, and after 2 months the mammary glands could be palpated on both sides, being about 10 mm in diameter and 2 mm thick. After 3 $^1/_2$ months of treatment the boy died from a sudden rupture of the myelomeningocele. At this time, the pigmentation of areolae mammae and linea abdominalis was intense, the mammary enlargement had shown further increase and pubic hair was present over a semicircular area with a radius of about 15 mm above the base of the penis. Post mortem examination of the mammary tissue showed, in addition to the gross enlargement of the glands, a microscopic proliferation of the efferent ducts among rich connective tissue (Figure 7). There were no glandular acini and, consequently, no functional signs. The pituitary, suprarenals and testes were normal.

Discussion

That synthetic estrogens of the stilbestrol type are readily absorbed through the skin is a well established fact. FITZSIMMONS (1944) pointed out that drugs of this group may cause gynaecomastia in male adults

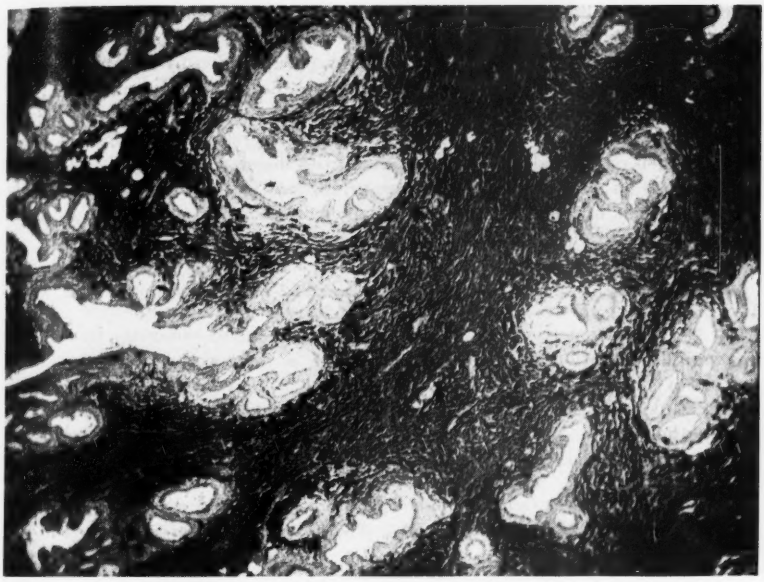

Fig. 7. Photomicrograph of mammary tissue.

through percutaneous absorption. She found 20 cases of mammary enlargement among 38 workers, employed in the manufacture of stilbestrol with an apparent risk of percutaneous absorption. In two of her cases, stimulation of mammary activity was established by biopsy.

An analogous mechanism seems responsible for the development of the mammary enlargement in the first patient, whose symptoms became evident and increased during exposure to stilbestrol, and later on diminished and disappeared, when exposure to the drug was stopped. This origin of the syndrome can be regarded as proven, as it has been reproduced in another case. The quantities of absorbed estrogen necessary to bring on the disturbance seem to have been so small that they do not give measurable urinary output of estrogenic substances.

In considering the mechanism of mammary enlargement, one can assume a direct estrogen action on the glandular tissue, which is sensitized by some pituitary factor (FOLLEY and MALPRESS, 1948), with the pituitary, in its turn, possibly activated by the estrogen. The pigmentation of areolae mammae, linea abdominalis and the genital organs, which is known to be caused by estrogens, may also have a similar mode of development. This seems apparent from the observations, made by

DAVIS and collaborators (1945), when treating adult females with estrogens. Their findings suggest a direct pigmenting action of estrogen without intermediation by other elements. Cooperation by the pituitary is, however, assumed and seems probable because no pigmentation appears when menopausal women are treated with estrogen.

A stimulation of the system of internal secretion to an increased androgen output, although not in quantities necessary to give increased amounts of 17-keto-steroids in the urine, may be assumed to be the explanation of the growth of sexual hair, which is a characteristic feature of the syndrome described in this paper.

Summary

A boy, aged 10 months, showed a progressive gynaecomastia, increasing pigmentation of areolae mammae, penis and scrotum, and growth of sexual hair. The symptoms were caused by percutaneous absorption of stilbestrol. The identical picture was demonstrated experimentally in another case. — The mechanism of development of the syndrome is briefly discussed.

Quelques résultats concernant une maturation sexuelle précoce chez un enfant du sexe masculin et provoquée par des onctions faites avec une substance oestrogène.

Un garçon de 10 mois présenta une gynecomastie progressive, une pigmentation croissante des aréoles des seins, du pénis et du scrotum, de méme que l'apparition de poils sexuels. Ces symptomes furent provoqués par l'absorbtion percutanée de stilbestrol. Ce tableau clinique put être mis en évidence expérimentalement dans un autre cas. Le mécanisme de développement de ce syndrome est brièvement discuté.

Einige Mitteilungen über geschlechtliche Frühreife bei einem männlichen Säugling, welche durch östrogene Salbe verursacht wurde.

Ein 10 Monate alter Knabe wies eine fortschreitende Gynäkomastie, zunehmende Färbung des Warzenhofes, Gliedes und Hodensackes sowie Geschlechtsbehaarung auf. Eine Aufsaugung von Stilböstrol durch die Haut hatte diese Symptome verursacht. Experimentell wurde das gleiche Bild in einem anderen Falle gezeigt. Der Entwicklungsmechanismus des Symptomenkomplexes wird in Kürze besprochen.

Algunos caracteres de precocidad sexual en un lactante debidos al empleo de un unguento con estrógenos.

Un niño de 10 meses mostró una ginecomastia progresiva con pigmentación aumentada de las areolas mamarias, pene y escroto y crecimiento del vello sexual, síntomas que eran debidos a la absorción por via

percutánea de un preparado de estilboestrol. Un cuadro análogo pudo demostrarse experimentalmente en otro caso. Se discute brevemente el mecanismo de desarrollo de este síndrome.

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Traumatic Heart Disease in a 6-Year Old Girl

by

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Non-penetrating traumatic injury to the chest, and sometimes even injuries to other parts of the body, may cause lesions of the heart. Death may follow (e. g. from rupture of the heart or of the great vessels); this may happen either immediately, or a few hours or even days after the injury.

Sometimes cases with a protracted course are seen, where death occurs after a longer period, or where the lesion is not fatal.

A case of this type was first published in 1676 by OLUF BORCH; the patient was an 8-year old boy who fell ill after a blow in the chest and died a few months later; on autopsy a lesion of the right auricle was found.

After this publication a number of similar cases, with a protracted course, have been reported. Reviewing the literature, WARBURG found 197 cases, and in addition published 6 cases of his own. Valvular lesions were not included in this series, as the traumatic origin is always difficult to establish in such cases.

Recently, an additional number of cases have been reported (ARENBERG, BARBER, SIGLER, KARTAGENER, NÄSLUND, and others).

The frequency of these lesions is by far the greatest in adult men, due to their greater exposure than women and children to injuries.

Myocardial lesion of this kind produces practically all sorts of myocardial symptoms. Most frequent are perpetual arrhythmia and angina pectoris. Nodal rhythm and various kinds of block are not uncommon, and cases of paroxysmal tachycardia and extrasystoles have also been reported.

ARENBERG and others have found that electrocardiographical signs of myocardial damage without other signs of heart disease are not infrequently met with in cases of chest injury.

Case record

U. K., a 6-year old girl, previously healthy, with no history of previous heart desease. In June 1950, an older child struck her on the precordium with his fist. She immediately turned pale and asked to be put to bed, but an hour later she wanted to get up and play again. During the following period she displayed less activity than usual and complained from pain in the epigastrium, and became dyspneic on slight exertion. She had a few attacks of pallor and dizziness, and once she collapsed during an attack. No cyanosis or fever was observed.

In September, 1950, she contracted tonsillitis and was admitted to the Blegdam Hospital, Department of Infectious Diseases, where a heart disease was revealed. She was then transferred to the University Clinic of Pediatrics, Rigshospitalet, where she stayed from October 7, 1950, to April 16, 1951 (J. no. 862/50).

On admission, no cyanosis or dyspnea was observed when she was resting, but she became dyspneic on slight exertion. The apical impulse was palpated in anterior axillary line. The heart beat was regular, about 120 per minute. Over the middle precordium a gallop rhythm was heard. No edema or signs of congestion of liver or lungs were found. The sedimentation rate, hemoglobin, leukocyte count, and antistreptolysin titer were normal. The Wassermann reaction was negative, and urine analysis revealed nothing abnormal.

On radiological examination the heart was found to be diffusely enlarged, the apex almost reaching the lateral chest wall (Fig. 1). Kymography showed little pulsation of the left ventricle, indicating inadequate emptying during systole.

The electrocardiogram showed on the first records a regular rhythm with abnormal ventricular complexes (rather broad initial complexes, though seldom more than 0.1 sec., and inversion of T_1) as well as an abnormal location of the P waves in the heart cycle. Each of these

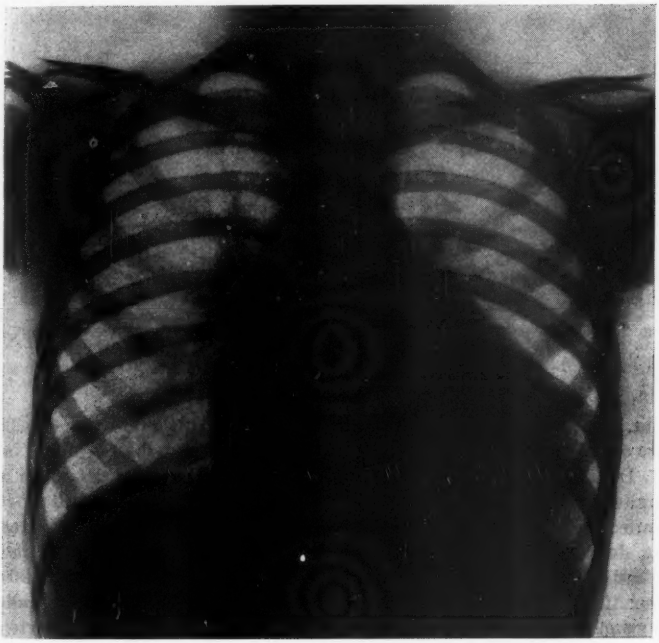

Fig. 1. Roentgenogram on admission, showing diffuse enlargement of the heart.

was apparently connected to a ventricular complex, in most instances occurring just after the initial complex, and sometimes coinciding with this (Fig. 2).

Later, however, it became evident that there was a disparity between the P rhythm and the ventricular rhythm, the latter being the faster. This was most clearly seen during digitalis therapy which decreased the rate of the P waves without noticeably influencing the ventricular rhythm. Both rhythms were still regular, but the ventricular complexes were completely independent of the P waves (Fig. 3).

Because of increasing cardiac insufficiency, with dyspnea, cyanosis and swelling of the liver, digitalis was administered from Oct. 31. The saturation dose was 40 cg and the maintenance dose 5 cg daily for five days each week. After some days of digitalis treatment short periods of sinus rhythm appeared, with upright T_1 and increased PQ intervals. It was, however, impossible to maintain a permanent sinus rhythm. Moreover, the sinus rhythm produced with digitalis apparently was too slow

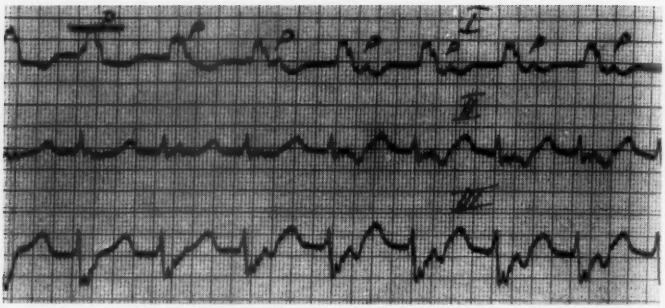

Fig. 2. Electrocardiogram taken on admission. The P waves occur after, or simultaneously with, the initial complexes.

(abt. 78 beats per minute) and the patient became tired and dyspneic. The size of the heart did not decrease. Digitalis therapy was discontinued Nov. 27. Dec. 20 a bronchopneumonia was treated successfully with penicillin. Digitalis therapy resumed Dec. 20 in the same dosage as before still proved ineffective, and from Jan. 13, 1951, quinidine was administered in increasing doses. Digitalis was withdrawn Jan. 16. Quinidine proved more effective, a constant sinus rhythm being obtained with a dosage of 30 cg four times daily. This dosage was therefore maintained. The gallop rhythm disappeared and the size of the heart decreased to some extent, though not to the normal. Complete normalisation of the electrocardiogram was not seen, however (Fig. 4). At first, ST_2 and ST_3 were depressed. After a few weeks this subsided, but simultaneously an inversion of T_1 appeared. The complexes slowly underwent alterations, and this was also true of the abnormal ventricular complexes of ectopic origin observed before sinus rhythm was established.

Before and during the quinidine treatment she had a few attacks of collapse, with pallor and impalpable pulse, of two or three minutes' duration. These attacks, probably of syncopal nature, subsided spontaneously on each occasion, before an electrocardiogram could be recorded.

As an attempt to influence the myocardial lesion, ACTH was administered from March 3 to March 22, 1951, in a dosage of 24 mg daily, divided into four intramuscular injections with 6-hour intervals. After 7 days of ACTH treatment the quinidine dosage was reduced, but this made the tachycardia reappear, and it was found that sinus rhythm could not be maintained on a lower quinidine dosage than prior to the ACTH treatment.

After dischargement she is still under treatment with quinidine in the dosage mentioned above. Tachycardia and dyspnea may occur when

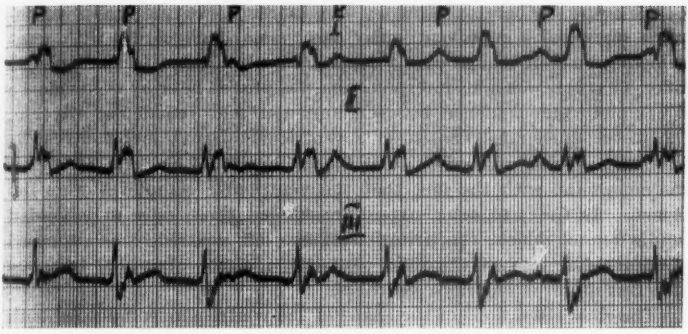

Fig. 3. Electrocardiogram during digitalis treatment (3/1 51). Complete atrioventricular block and ventricular complexes resembling those present in left-sided bundle branch block.

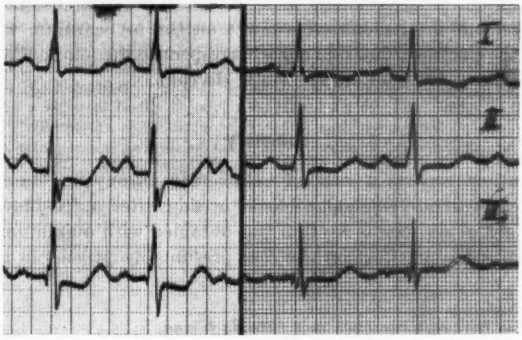

Fig. 4. Sinus rhythm obtained by quinidine (27/3 and 12/4 51). Note the alteration of the S—T interval.

she is playing too vigorously, but these symptoms disappear after a short rest. At long intervals she has short attacks of collapse of the same appearance as earlier.

Discussion

There can be no doubt as to the traumatic origin of the heart disease in this case, the symptoms having started immediately after an injury of the chest in a patient without any history of previous heart disease, and without any signs of infection or rheumatic fever.

As to the disturbance of myocardial function, the first electrocardiograms suggested a supraventricular paroxysmal tachycardia with wandering pacemaker, though with a dominant centre in the atrio-ventricular node. That this was a misinterpretation was proved later by the evidence of complete independence between auricular and ventricular rhythm. The disturbance must consist of a ventricular paroxysmal tachycardia combined with an atrio-ventricular block (functional block?). This view was consonant with the fact that the ventricular complexes were deformed. As they, to some extent, resembled those seen in left-sided bundle branch block, the irritation of the left ventricle was supposed to occur after that of the right ventricle, i. e. the abnormal impulses had their origin in the right ventricle.

The slow alterations of the shape of the ventricular complexes, both the ectopic ones during tachycardia and those seen after obtainment of sinus rhythm, were connected with reparatory processes in the myocardium, probably formation of scar tissue.

As shrinkage of scars on the skin has been observed during ACTH therapy (BRØCHNER-MORTENSEN & al.), ACTH was adminstered in the present case, but no demonstrable effect on the myocardium was seen, neither on the electrocardiogram nor with respect to the minimal quinidine dosage necessary for maintaining sinus rhythm.

Summary

The author reports a case of ventricular paroxysmal tachycardia combined with atrio-ventricular block, arising after a fist-blow in the chest in a girl of six. Sinus rhythm was obtained with quinidine. ACTH had no demonstrable effect on the scar presumably present in the right ventricle.

Cardiopathie traumatique chez une fille de 6 ans.

L'auteur rapporte le cas d'une tachycardie ventriculaire paroxystique liée à un bloc auriculo-ventriculaire, survenant après un coup de poing porté sur le thorax d'une petite fille de 6 ans. La quinidine produisit un rythme sinusal. L'ACTH n'eut aucune action sur la cicatrice présumée du ventricule droit.

Traumatische Herzerkrankung bei einem 6-jährigen Mädchen.

Der Verfasser beschreibt einen Fall von ventrikulärer paroxysmaler Tachykardie verbunden mit atrio-ventrikulärer Blockierung, welche nach einem Faustschlag auf die Brust bei einem 6-jährigen Mädchen entstanden war. Sinusrhythm wurde mit Chinidin erreicht. ACTH hatte keine sichtbare Wirkung auf die vermutlich in der rechten Herzkammer vorhandene Narbe.

Lesión cardiaca de origen traumático en una niña de 6 años.

El autor comunica un caso de taquicardia paroxística ventricular combinada con un bloqueo atrio-ventricular, trastornos que aparecieron tras recibir un puñetazo en el torax una niña de 6 años. Con la administración de quinidina se restableció el ritmo sinusal. El ACTH no produjo ningún efecto demostrable sobre la cicatriz que probablemente existía en el ventrículo derecho.

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PROGRESS IN PEDIATRICS

Erziehungsprobleme in einem Kinderkrankenhaus[1]

von

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Man lässt die Kinder in die Schule gehen, wenn sie schulreif, d. h. der Aufgabe gewachsen sind, die dort an sie gestellt wird: Von ihrer Mutter getrennt zu sein, dieselbe Lehrerin mit anderen Kindern zu haben, mit Gleichaltrigen umzugehen, die Fähigkeit zur Rezeptivität zu besitzen, was eine aktive Aufmerksamkeit voraussetzt. Alter und Schulreife fallen nicht immer zusammen, man hält aber die Schulreife für wichtiger als das Alter. — In die Kinderkrankenhäuser werden die Kinder geschickt, wenn sie krank sind, gleichgültig ob sie spitalreif, d. h. dem Aufenthalt im Krankenhaus und allen damit verbundenen Schwierigkeiten gewachsen sind oder nicht. Krankheit kann alle Kinder treffen. Die empfindlichen Kinder zeigen oft bei derselben Krankheit eine mehr alarmierende Symptomflora als die psychisch robusteren Kinder. Es kommt daher vor, dass viele empfindliche Kinder wegen einer Krankheit ins Krankenhaus kommen, die bei einem psychisch stabileren Kind keinen Anlass zur Aufnahme ins Krankenhaus gebildet hätte.

Angesichts der Tatsache, dass viele Kinder gepflegt werden müssen, die psychisch nicht spitalreif, d. h. reif für Trennung von ihrer Mutter, sind, müssen die Kinderkrankenhäuser über die nötigen Mittel verfügen, welche die psychischen Schäden, denen das Kind ausgesetzt wird, soweit wie möglich mindern können. Dies gilt für solche Kinder, die sich in Bezug auf Krankenhausschäden in einem empirisch festgestellten vulnerablen Alter

[1] Einleitungsvortrag auf dem Internationalen Pädiatrischen Kongress Zürich 1950/Kinderpsychiatrische Sektion.

befinden; ferner solche Kinder, deren Leben im Elternhaus von der Art war, dass eine Trennung von demselben als eine Verletzung empfunden wird, selbst wenn das sog. vulnerable Alter bereits überschritten ist. Es kann sich dabei um ein älteres Kind handeln, das sich gerade in einer akuten Dethronisierungslage befindet. Beim Eintreten der Krankheit kann eine schwere emotionelle Störung zwischen Mutter und Kind geherrscht haben, die dazu beigetragen hat, dass die Trennung schmerzlicher wird und vom Kind als ein Racheakt seiner Mutter aufgefasst wird. Es kann im Elternhaus eine latente Ehescheidungsstimmung vorhanden sein, wobei der eine Partner in Anwesenheit des Kindes dem anderen gegenüber offen aggressiv auftrat, wobei aber doch die Anwesenheit des Kindes einen hemmenden Einfluss ausübte. Hier kann das Kind instinktiv fühlen, dass man es zu Hause braucht und es hat Angst davor, was zu Hause geschehen kann, wenn es fort ist.

Dies sind nur einige wenige Beispiele dafür, wie verschieden der phychologische Hintergrund für die Aufnahme ins Krankenhaus sein kann und wie wichtig es ist, dass man diesen etwas kennt, um das Verhalten eines Kindes während der ersten Zeit seines Krankenhausaufenthaltes richtig verstehen zu können. Man kann daher nicht von einer einheitlichen Erziehungslage im Kinderkrankenhaus reden, es handelt sich hier vielmehr um eine ausserordentlich weitgehende Individualisierung bei der Behandlung der Kinder, unter Berücksichtigung der primären Bedürfnisse der Kinder, auch der psychologischen und vor allen Dingen der emotionellen.

Wenn ein Kind erkrankt, wird es hilflos und bedarf der Hilfe seiner Mutter mehr als sonst. Eine Mutter wird wohl immer mehr oder weniger unruhig, wenn ihr Kind krank wird. Ihre Unruhe drückt sich in einem stärkeren Bedürfnis zum Pflegen und Schützen des Kindes aus. In dieser Lage muss eine Trennung von Mutter und Kind infolge einer Aufnahme ins Krankenhaus auf beide Partner angstmobilisierend wirken. Bei beiden ist eine gesteigerte Angstbereitschaft vorhanden. Das Kind kommt ins Krankenhaus und versucht vielleicht, — gerade wenn es in einer Zeit fremden Menschen ausgeliefert ist, in der es die Hilfe seiner

Mutter am meisten nötig hätte, — seine Gefühle mehr oder weniger zu verbergen.

Das Kind fühlt sich verlassen, und aus dieser Lage können sich verschiedene Muster des Verhaltens herauskristallisieren. Gerade auf das gut erzogene Kind macht die Krankenschwester den Arzt aufmerksam, weil es so komisch gut erzogen ist. Auf alle an ein solches Kind gerichteten Fragen antwortet dies „Nein, danke" oder „Ja, danke", „das macht nichts" und bei Untersuchungen: „Nein, es tut gar nicht weh, darf ich jetzt nach Hause fahren?" ein für ein vierjähriges Kind vollständig unnatürliches Auftreten, das von der betreffenden Krankenschwester als komisch aufgefasst wird, das aber in Wirklichkeit eine furchtbare Tragödie ist. Das Kind ist dermassen von Angst erfüllt, dass es sich gegen Niemanden zu opponieren wagt, dass es sich überhaupt nichts zu tun getraut, was eventuell sein Ansehen bei dem erwachsenen Menschen herabsetzen könnte. Es versucht durch sein Benehmen möglichst beliebt zu werden, was für das Kind bedeutet, dass es nach Hause geschickt werden kann und nicht weiter in der Weise bestraft wird, dass es in einem Krankenhaus bleiben muss.

Oder ein anderes Kind, das unmittelbar nach der Ankunft ständig „Mama, Mama, Papa, Papa, Grossmutter, Grossmutter!" usw. ruft, das durch sein lautes Geschrei die ganze Abteilung stört. Es glaubt noch an seine eigene magische Macht, die Personen, die es vermisst, herbeilocken zu können. So sucht sich die Angst des Kindes auf verschiedenen Wegen einen Auslauf.

Die zu Hause sitzende Mutter sucht ebenfalls einen Auslauf für ihre Unruhe, sie ruft zu unpassender Zeit das Krankenhaus an, sie stört den Arzt mit unnötigen Fragen usw. Je unvollständiger und routinemässiger die Auskünfte sind, die ihr erteilt werden, desto mehr bildet sie sich ein, dass ihr Kind ausgeliefert sei, was ihre Unruhe steigert. Der Kern der Erziehungsprobleme in einem Kinderkrankenhaus ist ausser der Erziehung des einzelnen Kindes die Kenntnis und das Verständnis für die biologische Wechselwirkung zwischen Mutter und Kind. Versteht man die Bedeutung dieser Tatsache und handelt danach, so werden die Kinder im Kinderkrankenhaus sicher leichter behandelt werden

können und brauchen unter dem Aufenthalt im Krankenhaus weniger zu leiden

Manche Kinderärzte sind der Ansicht, dass man, wenn das Kind einmal im Krankenhaus aufgenommen ist, alles tun muss, um nie von den Eltern des Kindes zu reden, da sonst das Denken an diese und an das Elternhaus den ganzen Umstellumgsprozess vom Elternhauskind zum Krankenhauskind verlängert. Persönlich glaube ich, dass man je eher, je lieber eine Brücke zwischen dem Elternhaus und dem Krankenhaus schlagen soll, und zwar in erster Linie auf die Art und Weise, dass die Krankenschwester, die das Kind pflegen soll, dieses fragt, „wie Mama es gewöhnlich macht" usw. Das Kind bekommt dann bald Assoziationen zwischen der Person, die seine Ersatzmutter sein soll, und seiner eigenen Mutter.

Ferner sollten die Besuche von Angehörigen individualisiert werden. Manche Kinder, z. B. besonders die im vulnerablen Alter befindlichen, dürfen nicht, was den kontakt mit ihren Eltern betrifft, zu stark abgesperrt werden. Die Besuche von Angehörigen dürfen nicht vom Personal als ein notwendiges Übel betrachtet werden. Das Personal muss vielmehr versuchen, sich die Auffassung dieser Besuche seitens der Kinder anzueignen. Obgleich die Besuche Unruhe, Verzweiflung und Tränen bei Kindern und Müttern hervorrufen, können sie dennoch ein Sicherheitsventil sein, das für beide Partner einen wichtigen mentalhygienischen Faktor bildet.

Wir haben die eingewurzelte Vorstellung, dass Gefühlsausbrüche, besonders für Kinder, etwas Schädliches sind. Wir wissen, dass bereits 2 — 3jährige Kinder eine ungeheure Fähigkeit besitzen, Gefühle zu verdrängen, sie unter einer guterzogenen Fasade zu maskieren. Für diese Kinder kann es ausserordentlich wichtig sein, dass sie dann und wann sich getrauen, ihre Gefühle zu zeigen, dass sie es wagen, ihrer Unzufriedenheit mit ihrer Mutter freien Spielraum zu geben. Die Verzweiflung der Mütter wenn sie bei ihrem ersten Besuch mit einem „geh fort!" begrüsst werden, muss ihnen erklärt werden. Der Ausruf des Kindes ist nur ein Ausdruck seines dadurch verursachten Rachegefühles, dass es ausgeliefert worden ist, gewissermassen eine Bestrafung der Mut-

ter. Wenn die Mütter den Ausruf ernst nehmen und eventuell dem Kind Vorwürfe machen, wird die Lage nicht besser.

Wenn die Kinder ein Gespräch mit dem Personal einleiten, haben sie eine bewusste oder unbewusste Absicht damit. Das Personal darf dann nicht die ganze Sache mit einem Wort abtun. Es kann sich nämlich dabei um Heimweh oder eine bevorstehende Operation handeln. In vielen Krankenhäusern für Erwachsene versucht man auch, den Weg einzuschlagen, dass man zerstreut und ablenkt anstatt die Sachen zu diskutieren, die für das kranke Kind oder den erwachsenen Patienten aktuelle Probleme bilden. Das Kind muss davon überzeugt werden, dass es keine Schande ist, Angst zu haben, dass auch erwachsene Menschen Angst haben. Das Kinderkrankenhaus muss die Angst des Kindes als eine selbstverständliche Realität akzeptieren, mit ihr rechnen und dem Kind helfen, die Angst zu überwinden, vielleicht in erster Linie in der Weise, dass das Kind das Gefühl bekommt, dass man im Krankenhaus ängstliche Kinder ebenso gern hat wie mutige. Mutige Kinder zu bevorrechten hat nur zur Folge, dass die ängstlichen Kinder versuchen, ihre Angst zu verbergen. Alles was an Gefühlen in diesen Jahren verborgen wird, wird vergrössert und die Lage der Kinder wird erschwert. Obwohl die Angst bei Kindern im Vorschulalter offener zu Tage tritt, kann sie doch während eines Aufenthaltes im Krankenhaus auch in höheren Altersgruppen leicht mobilisiert werden.

Fragen intelligenter Kinder betreffs ihrer Krankheit dürfen nicht ignoriert werden. Wenn das Personal all die Anforderungen, welche die moderne Krankenhauspflege auch in Bezug auf die emotionellen primären Bedürfnisse der Kinder stellt, erfüllen soll, ist es ausserordentlich wichtig, dass eine richtige Auswahl des Personals getroffen wird. Das Personal ist der Faktor, der die freundliche Atmosphäre in einem Krankenhaus schaffen, der einigermassen die Angst der aufgenommenen Kinder und der daheimgebliebenen Mütter neutralisieren können soll. Das Personal muss sich für die Kinder interessieren, die Kinder lieben, nicht äusserlich, wobei die Liebe zu den Kindern dasselbe ist wie hätscheln und zärteln, sondern tiefer, d. h. es muss Kinder gern haben und genügend Interesse besitzen, um sich in die emotionellen

Bedürfnisse eines Kindes versetzen zu können. Nicht einmal das genügt. Das Personal muss ausserdem reif für die Zusammenarbeit mit erwachsenen Menschen, mit dem übrigen Personal und vor allem mit den Eltern sein. Es gibt viele neurotische Frauen, die aus Furcht vor der Welt der Erwachsenen die Welt der Kinder zu ihrem Arbeitsplatz gewählt haben; diese Frauen können genial sein, soweit es sich darum handelt, ein Kind zu verstehen, sobald aber die Zusammenarbeit mit den Eltern in Frage kommt, zeigen sich bedenkliche Mängel.

Aus dem oben gesagten geht hervor, dass die Erziehungsprobleme in einem Kinderkrankenhaus eng mit der individuellen Lebenssituation der einzelnen Kinder zusammenhängen. Soll deshalb jede aktive Erziehung, besonders für diejeningen Kinder, die lange Zeit im Krankenhaus liegen, vollständig eliminiert werden? Nein, keineswegs. Das Personal muss sich jedoch immer dessen bewusst sein, dass man das Vertrauen und die Anhänglichkeit eines Kindes nicht gewinnt, kein Gefühl der Sicherheit beim Kinde hervorruft, wenn man damit beginnt, es aktiv zu erziehen, ihm vorzuhalten was es tun und was es lassen soll. Hier wie in allen anderen alltäglichen Erziehungslagen muss man erst das Kind kennen lernen, das erzogen werden soll, danach den Kontakt mit dem betreffenden Kind herstellen und erst dann hat man das Recht, Anforderungen zu stellen.

Ferner ist es wichtig zu wissen, dass die eventuellen Erziehungsfehler, welche die Eltern begangen haben, und die sich in einem anomalen Benehmen des Kindes im Krankenhaus zeigen, nicht „während eines Aufenthaltes von ein paar Wochen im Krankenhaus beseitigt und korrigiert" werden können. Man muss sich vielmehr darüber im Klaren sein, dass eine Krankheit und die Hilfe, die das Kind während dieser Krankheit braucht, dem Kind in hohem Masse einen angenehmen Eindruck machen soll, und dass man daher alles tun muss, damit das Kind bei der Genesung nicht ein fixiertes Muster für sein Benehmen bekommen hat, das sich durch eine extreme Hilflosigkeit und ein opportunes Ausnützen seiner Lage als Patient kennzeichnet.

Alle Kinder lieben es, den Mittelpunkt der Ereignisse zu bilden. Auch kranke Kinder können sich schon sehr früh während der

Genesung allmählich selber helfen. Dabei kommt es ganz darauf an, wie dies geschieht, d. h. ob das Kind es als einen schmerzlichen Verzicht auf ein Vorrecht oder als einen Fortschritt in der Genesung empfindet. Für kleine Kinder, die lange im Krankenhaus liegen müssen, ist es ausserordentlich wichtig, dass das Personal immer wieder auf die Verantwortung hingewiesen wird, welche die Ersatzmutter hier tragen muss. Sie soll nicht nur die rein physischen und die emotionellen Bedürfnisse befriedigen, sondern sie soll auch der stimulierende Faktor sein, der garantiert, dass die intellektuelle Entwicklung des Kindes mit der physischen gleichen Schritt hält. Sie soll auch das Sprachvorbild sein, welches das Kind nachahmen soll. Fehlt das Sprachvorbild so verzögert sich die Sprachentwicklung. Sie soll die Wissbegierde des Kindes auch zu einem Zeitpunkt befriedigen, wo das Kind verbal keine Fragen stellen kann, sie soll sozusagen eine persönliche Atmosphäre um das Kind schaffen. In dem unpersönlichen, sterilen und routinemässigen Boden gedeiht weder die physische noch die psychische Entwicklung des Kindes.

Die Wissenschaft schreitet in der Pädiatrie wie in anderen Zweigen der Medizin fort, man muss sich aber fragen, ob die Pflege der kranken Kinder mit allem, was dies bedeutet, im selben Tempo vorwärts geht. Wenn auch vielleicht die Mehrheit der Kinder sozusagen spitalreif ist, d. h. den Aufenthalt im Krankenhaus ohne psychischen Schaden erträgt, so muss doch alles getan werden, damit die Minderheit von Kindern, die dazu veranlagt sind, mit Symptomen zu reagieren, die wir in dem Wort „Hospitalism" zusammenfassen, auch psychisch wohlbehalten nach der nötigen physischen Pflege unsere Kinderkrankenhäuser verlässt. Dies ist eine absolute Forderung, die man als Kinderpsychiatriker aufstellen muss. Das Personal, das kranke Kinder pflegen soll, muss zahlreich sein, es muss über genügend Zeit verfügen, eine Zeit, deren Anwendung sich nicht in rationellen Einheiten messen lässt, ebenso wenig nationalökonomisch in einer Effektivität, die dem registrierbaren, unmittelbar nachweisbaren Ergebnis entspricht. Wenn auch der äussere Rahmen eine grosse Rolle spielt, d. h. wie elternhausähnlich die Kinderabteilungen sind usw. so kann doch der äussere Standard des Krankenhauses niemals

dieselbe Rolle spielen wie die Qualität der Menschen, die unsere kranken Kinder pflegen sollen. Auf *ihre* Ausbildung muss Geld verwendet werden, wenn die Mütter das Gefühl bekommen sollen, dass ihre Kinder im Kinderkrankenhaus nicht *ausgeliefert*, sondern in *Obhut genommen* sind.

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Proceedings of the Section for Pediatrics and School Hygiene of the Swedish Medical Society

Meeting at Sundsvall, September 23, 1951.

Maj Danielsson: **A Comparison Between Clinical and Roentgenologic Diagnosis of Rickets.**

To ascertain whether rickets could be detected earlier by regular roentgen examinations X-rays of the right wrist of all children below the age of 2 years have been taken at one of the Children's Welfare Centres at Sundsvall. More than 500 examinations have been performed on 310 infants. In 11 cases, slight roentgen changes have been noted, but the serum values of calcium, phosphorus and phosphatase have been normal in all. In 2, slight physical findings were present. In 27 infants with normal X-rays, however, similar physical findings were recorded, such as craniotabes, prominence of the epiphyses, rosary and Harrison's groove. Two or more of these symptoms were found together in 6 children, but even in these the roentgen pictures were normal. Thus, in the present material no cases of rickets were detected by X-ray and it may be concluded that routine X-ray examination of infants at a Welfare Centre is unnecessary. Clinically suspicious cases should be X-rayed, however, and for this purpose Type I Centres should have X-rays available.

Gert von Sydow: **A 4 Years' Analysis of Rickets.**

78 cases of rickets, 64 of which were clinically, roentgenologically and serologically diagnosed as active, have been analysed from various points of view. The age at the time of the diagnosis of the active cases showed an extremely good correlation with the month of birth, thus confirming the significance of a deficiency of sunlight in the pathogenesis. With regard to sex, boys outnumbered girls by two to one, and in boys the age of onset was earlier. 31 of the 43 boys with active rickets were below the age of 10 months, against only 3 of the 21 girls. When cases with tetany are dealt with separately, the difference in sex distribution becomes even more marked. In the present limited group the findings suggest that in the pathogenesis of rickets there is an endogenous, possibly inherited factor whereby a moderate deficiency of vitamin D may render boys more liable to the disease. Other observations may also indicate such an endogenous factor, e. g. the fact that rachitic children are often manifestly small in stature, and that in some cases active rickets develops despite adequate prophylaxis.

Discussion.

T. Torstensson mentioned experiences that confirmed those of Dr. von Sydow, particularly as regards the sex distribution and he drew attention to the reluctance of doctors to prescribe sufficient doses of vitamin D. *B. Vahlquist:* I think we all agree that we have listened to two very interesting lectures. If the sex difference is proven in larger series it will be of interest to find an explanation. The following fact may be relevant: in his studies of the development of the osseus centres Dr. Elgenmark has shown that girls are definitely ahead of boys in this respect in the first years of life. One word concerning the anaemia in rickets; all the evidence suggests that this is not due to the rickets itself but to a co-existing iron deficiency and this should be treated accordingly. *A. Wallgren* said he had not much faith in the supposed advantages of routine X-ray examinations for rickets in infants at the Children's Welfare Centres. A positive roentgen finding is not an early sign. The sex distribution in Dr. von Sydow's material was extremely interesting; was an endocrine factor at work? *A. Myrgård* emphasized the importance of informing doctors in public health service of such findings in order to draw increased attention to prophylaxis. He asked to what social stratum the children belonged, suggesting that it was probably the lowest, where all prophylaxis is ignored. In his opinion, roentgen equipments at the Children's Welfare Centres would be superfluous, considering that X-ray examinations are rare, and that the hospitals to which the Children's Welfare Centres, Type I, are localized have special Roentgen Departments. *G. von Sydow* stated that a maximum of one third of the patients belonged to the lowest social stratum. After the return home of a mother from the maternity hospital, it is important to visit her as early as possible. In the Northern part of Sweden, prophylaxis with vitamin D is applied also in summer time.

Bo S. V. Bille: **Pseudo-hypoparathyroidism.**

Since *Albright* and others in 1942 described the first three cases of a syndrome which they called pseudohypoparathyroidism about fifteen cases have been published, though none from Scandinavia. The author gives an account of a case of pseudo-hypoparathyroidism in a girl aged 9 years, slightly mentally deficient, short and thickset in stature with a round face, stubby hands, short metacarpus (including all fingers but the index), soft tissue calcifications, hyperphosphatemia and hypocalcemia. She has an imbecile maternal uncle similarly affected.

(To be published in the Acta Paediatrica in 1952).

Gert von Sydow: **Lactation Prognosis and the Amount of Mother's Milk at the Maternity Hospital.**

An inquiry has been undertaken during a six months' period at Children's Welfare Centres regarding the duration of breast feeding in

infants returning home from the maternity clinics at Gothenburg. Infants with a birth weight below 3 kg, twins, infants that left the Children's Welfare Centre before the age of 2 months, as well as infants who had defects likely to affect their ability to suckle, have been excluded from the investigation. Mothers with inverted nipples or other defects have, however, not been eliminated, provided the infant was being given breast milk on discharge from the maternity hospital. The lactation regimen comprised a regular emptying of milk from the mammae after meals, four times a day, from the third day. Lactation time was defined as the time during which the infant was actually being breast fed in whole or in part. Infants who, on the sixth day of life, got a maximum of 200 ml of mother's milk, did not do well: 44.1 per cent being weaned before the age of 2 months and only 22.1 per cent continuing for 6 months or more. Of infants getting more than 200 ml on the sixth day only 0.6—6.6 per cent were weaned before the age of 2 months and 50—80 per cent received their mother's milk up to a minimum of 6 months. Infants from whose mothers, on the sixth day of the baby's life, a minimum of 100 ml of milk could be drawn, over and above the amount sucked by the infant, showed considerably better lactation times than the rest of the series. This applied to those who could themselves suck what they needed (i. e. a minimum of 300 ml), as well as to those who got a maximum of 200 ml. It would seem therefore that the lactation time could, in many instances, be improved by systematically emptying any milk remaining after the infant had suckled.

Discussion.

A. Wallgren stressed the importance of defining what exactly was meant by breast feeding. In the total series of the clientele of the Children's Welfare Centres in Sweden, the lactation frequency was strikingly lower than in Dr. von Sydow's material. *G. von Sydow:* Our figures refer to total lactation time, not to the time of exclusive breast feeding. The reasons why mothers with a considerable initial amount of milk dry up are, as a rule, to be found in social factors that have complicated the question of continued suckling.

Scientific Exhibition at Sundsvall's Children's Hospital (Dr Gert von Sydow).

Infant Mortality in the County of Västernorrland, 1928—50. Since 1928—33, and 1938—40, when Dr. Urban Hjärne studied infant mortality in the above-mentioned county, the death rate has steadily fallen, more rapidly than in Sweden as a whole. It is now lower than the Swedish average. The decrease is particularly marked in the industrial district of Njurunda, Skön's and Ljustorp's assize division. In 1928—30 the

death rate there amounted to 109.2 per mille and in 1950 had dropped to 11.4 per mille. The mortality during the 2nd—12th month of life was 62.8 per mille in 1928—30 and in 1950 3.2 per mille.

2. *Hereditary Deforming Chondrodysplasia* (multiple exostoses, diaphyseal aplasia). Noted in 6 persons of four successive generations. In the youngest patient, the changes have been subject to observation since birth.

3. *Accumulated Cases of Renal Insufficiency in a Family with Repeated Intermarriages.* The grandparents were cousins, the parents likewise cousins, and 6 of 9 brothers and sisters have suffered from severe renal insufficiency. So far, it has caused 5 deaths. Autopsy in one case disclosed a marked fibrosis and small cysts in the kidneys. A paternal uncle of these children is married to their maternal aunt. Several of their 9 children are imbecile, though showing no signs of renal disease.

4. *Chronic Recurrent Celiac Disease in a 15 Years Old Patient* of dwarfish growth and multiple symptoms of deficiency, such as anaemia, rickets, hypovitaminosis A, C and K, and hormonal disturbance.

5. *Rickets with Spontaneous Fracture and Tetany* in celiac disease.

6. *Congenital Toxoplasmosis with Severe Changes in Various Organs.*

7. *Six Cases of Tuberculous Meningitis.* 4 of these cases had been treated with streptomycin and are living, one 3 $^1/_2$ years after the onset of the meningitis.

8. *Six Cases of Tularemia.* All six were diagnosed in September—October 1950. Five came from the same community. All began with a slow-healing wound on one leg (suggestive of an insect's bite) and regional lymphadenitis.

9. *Bronchitic Asthma.* 29 of 39 patients have reacted positively to allergen tests. 19 have been treated with specific hyposensitization and observed for a minimum of six months. 10 have become free from symptoms or improved. Result unknown in 3 cases.

10. *Cerebral Tumours Diagnosed in 1947—1950.* 5 cases. 2 of these patients are alive, subjectively healthy, 3 $^1/_2$ and 2 $^1/_2$ years after operation. In both the tumour was an astrocytoma, one in the cerebellum and the other in the roof of the fourth ventricle. The other tumours were an ependymoma and a glioma.

11. *Renal Tumours Diagnosed in 1948—1951.* 5 cases. All have died. 3 cases of renal adenosarcoma were operated upon, dying after metastasizing in various organs, within from 5 weeks to 11 months after the operation.

NEWS AND COMMENTS

From October 11th to October 13th, 1951, there was held in Zürich under the chairmanship of Professor G. Fanconi, Zürich, Secretary General, International Paediatric Association, a Conference on Paediatric Abstracts. Present at the meeting were representatives of National Pediatric Societies and Pediatric Journals.

The Conference decided unanimously to send the following suggestions to the presidents of national paediatric associations, and to the editors and publishers of paediatric journals, requesting them to publish them either partly or in extenso:

1) In various meetings of UNESCO, World Health Organization, etc., there have been many discussions of ways in which to coordinate medical literature and particularly the various abstract journals. As a result of these discussions the suggestion was put forward at the 6th International Congress of Paediatrics by different members that an attempt should be made to coordinate the abstract journals in paediatrics.

With regard to the 3 abstract journals that were represented at the Conference ("Excerpta Medica, Section on Paediatrics" in English, "Courrier du Centre International de l'Enfance" in French and English, and "Zentralblatt für Kinderheilkunde", edited by Springer, in German) it is suggested that the following special fields of all these journals should be defined: "Courrier" should continue publishing indicative abstracts in French and English, by which the reader is quickly informed about publications appearing all over the world. "Excerpta Medica, Section on Paediatrics" and "Zentralblatt für Kinderheilkunde" should, on the other hand, publish informative abstracts. Unimportant publications should of course be abstracted very briefly or not be mentioned at all.

2) The discussions at the Conference proved that abstracting is a very difficult task. Authors' abstracts are as a rule subjective and not objective. On the other hand, abstracts of others are often uneven in quality and may omit important data. The attempt should therefore be made to encourage leaders in paediatrics such as directors of paediatric clinics, newborn infant services and research foundations to send directly to the publishers of the 3 mentioned abstract journals notifications of significant or especially important articles emanating from their clinics or services, from other university clinics or research foundations of their town. It is understood that the ultimate discussion as to the use of such notifications will rest with the editors.

3) In order to promote wider dissemination of knowledge regarding advances in paediatrics throughout the world, the publishers of "Ex-

cerpta Medica, Section on Paediatrics", "Zentralblatt für Kinderheilkunde" and "Courrier" are requested to grant to the paediatric groups of certain nations free of charge the use of 10 abstracts monthly or 120 abstracts annually for publication and dissemination in their own language. This material shall not be circulated for financial profit. In the first instance the following nations should be considered: Finland, Iceland, Greece, Turkey, China, Japan. Each national group must make its own separate agreement with the individual abstract publishers and also notify the Secretary General of the International Paediatric Association of any arrangement concluded.

4) In order to aid the Spanish, Italian and Portuguese paediatric groups to create abstract journals, the Conference suggests that the publishers and editors of these language groups should seek an agreement with "Excerpta Medica, Section on Paediatrics", "Zentralblatt für Kinderheilkunde" or "Courrier" that authority for complete or partial translation is put at their disposal. The Executive Board of the International Paediatric Association through the Secretary General should be kept informed about these agreements and exercise its efforts to secure the widest possible use of such facilities.

5) The Conference hopes that by adopting these suggestions already made national paediatric associations should consider the possibility of discontinuing the publication of abstracts in all their journals in order to avoid unnecessary duplication and expense.

6) It is suggested that the publishers of paediatric journals in infrequently used languages should provide each article with a summary in English, French, German, Russian and Spanish, including complete translation of the title.

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BOOK REVIEWS

ERWIN THOMAS: *Die innersekretorischen Krankheiten des Kindes und ihre Behandlung.* Ferdinand Enke, Publisher, Stuttgart, Germany, 1951. Price DM 12.40.

There are very few books dealing exclusively with Paediatric Endocrinology but recently there has been an addition in the form of a supplement in the Archiv für Kinderheilkunde, number 26. by the well known German paediatrician E. Thomas. It is a great pity that the author has not tried to emphazise the more important references in his text, and

thus saved the average reader an unnecessary amount of useless reading. The paucity of illustrations is also to be deprecated. This supplement cannot be regarded as an introduction to Paediatric Endocrinology but should be reserved for the more advanced reader interested in endocrine diseases in childhood. Those who are looking for information about older and more recent European work in this special field will find the book of considerable value.

C. G. Bergstrand. Stockholm.

O. GÖRGÉNYI-GÖTTCHE: *Tuberkulose im Kindesalter.* Springer-Verlag, Wien, 1951. Price DM 34.80.

In this monograph the author gives an extensive presentation of the outlines of tuberculous infection in childhood. An account is given of the diagnosis of tuberculous disease, pathologic anatomy and clinical picture of different manifestations and stages of tuberculous infection and the differential diagnosis in relation to other non-tuberculous pulmonary diseases. The two last chapters deal with prophylactic measures and general principles for treatment including chemotherapy and antibiotics. The great experience and knowledge of the author makes this book a valuable contribution in this field. His main interest is concentrated upon the erosion of hilar gland into the bronchi and its relation to "epituberculosis". His work on this problem together with the otologist KASSAY and the pathologist KÁLLÓ is well-known. The presentation is illustrated by detailed case reports and several X-ray pictures. Unfortunately these pictures are not of the highest quality, the reproductions are small and not clear. In the bibliography only the more important references are given. It might have been of value if this list had included all references in the text. These critical remarks do not diminish the value of this book as an excellent guide to the pediatrician interested in childhood tuberculosis.

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